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THE INFLUENCE OF THE VINEBERG SPONGE OPERATION UPON THE HYDROSTATICS OF THE MYOCARDIAL CIRCULATION IN HEALTH AND DISEASE: EVIDENCE OF LUMINAL VENTRICULAR CIRCULATION IN THE BEATING HEART*

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THE TERM "myocardial circulation" in preference to "coronary circulation" has been introduced because life depends upon a healthy myocardial circulation, no matter what its source. Recent experimental and clinical evidence observed at McGill University and at the Royal Victoria Hospital, Montreal, suggests that under certain conditions the myocardium is capable of drawing oxygenated blood into itself from both extracardiac and intracardiac sources.

In the past 16 years, during our studies to improve the myocardial circulation in both the animal and human ischemic heart, certain facts have been established which have led to our present concepts on this subject.

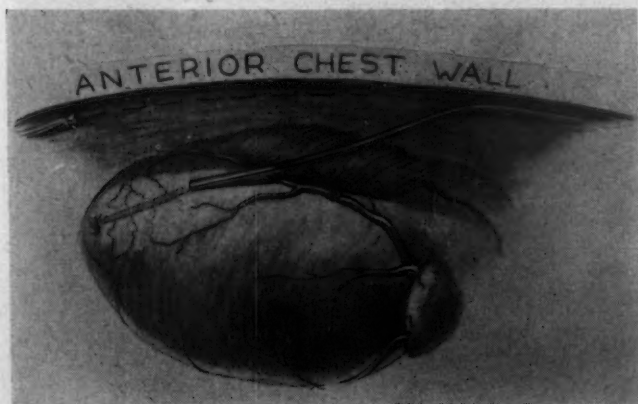


Fig. 1.—Schematic drawing of internal mammary artery implantation.

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In 1945, a systemic artery was detached from the chest wall and implanted into an animal's heart where it remained patent (Fig. 1), and in 1950 the same result was obtained after the internal mammary artery was implanted into a human heart. The implanted internal mammary artery was placed within a tunnel made in the wall of the

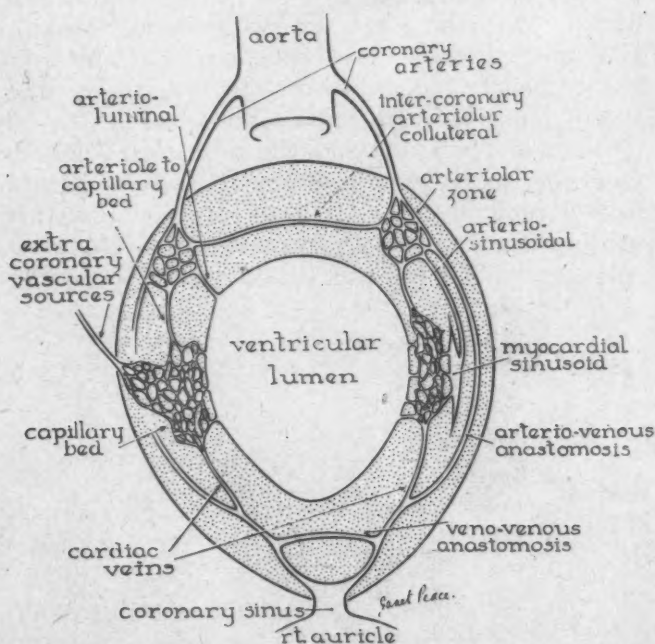


Fig. 2.—Wearn's and the senior author's concept of myocardial circulation.

left ventricle, with either its end or side branches open and bleeding. Much to our surprise these implanted arteries not only remained open but the blood which escaped from their ends or branches never formed a hematoma within the tunnel made in the wall of the left ventricle.

In our early experiments we studied the problem of arterial implantation and placed a femoral artery into a tunnel made in the adductor muscle in the animal, leaving the artery branches open and bleeding. In every case a hematoma was formed and the artery invariably became blocked. These facts led us to a more complete study of the myocardium and its structure, in the course of which the fine work of an early investigator was revealed.

The work of Wearn,¹ performed many years before, outlined a vast network of myocardial vascular spaces (Fig. 2). Wearn described the coronary

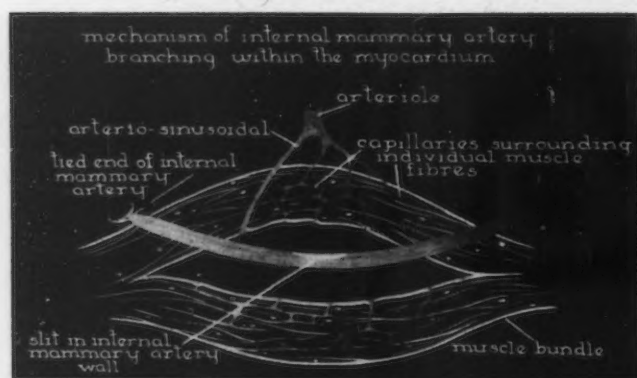
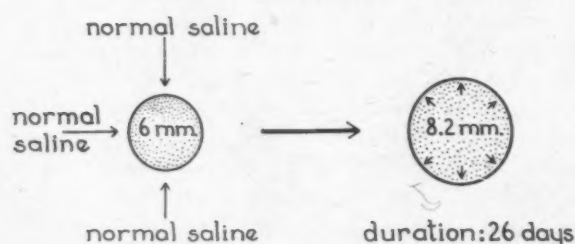


Fig. 3.—Drawing of internal mammary artery implant lying in a myocardial sinusoidal space.

arteries dividing into a series of arterioles which were distributed as follows: (1) to a capillary network which directly surrounds myocardial fibres, as similar networks surround muscle fibres in other parts of the body; (2) directly into the ventricular lumen, which he terms arteriolar luminal vessels; (3) arteriole-to-other-arterioles, which are now termed collaterals; and (4) directly to large vascular spaces lying between muscle fibre bundles called *myocardial sinusoids*, and the arterioles going to them he terms *arteriosinusoidal vessels*. Wearn further pointed out that the myocardial sinusoids were in direct communication with the left ventricular cavity. The presence of a myocardial sinusoid

1. plain casein plastic rod:



II ameroid coronary artery constrictor:

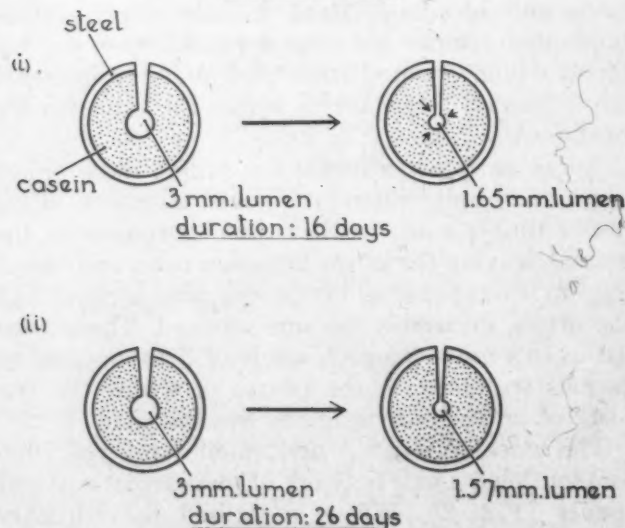


Fig. 4a.—Casein plastic rod with central lumen and peripheral slot contained within steel jacket.

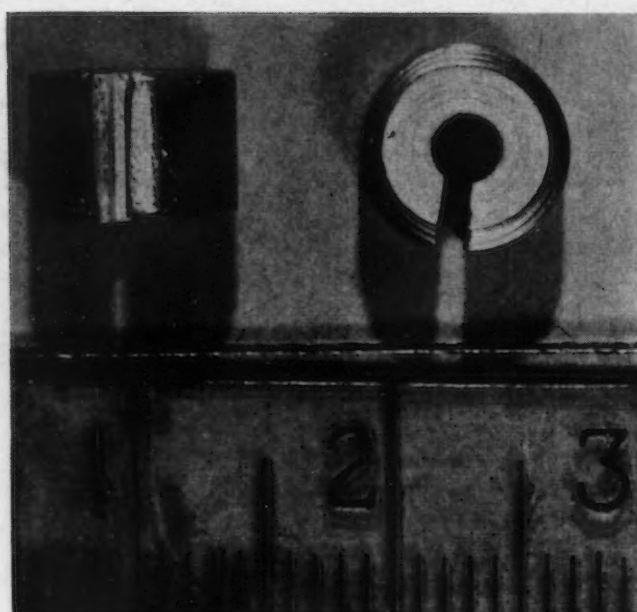


Fig. 4b.—Close-up view of ameroid constrictor.

explained why a bleeding systemic artery implanted into a tunnel made in the myocardium remained open and why there was no hematoma formed in the ventricular wall. It would appear that when the tunnel was made in the left ventricular wall using an artery forceps, the myocardial sinusoids were broken into, thus providing a rapid run-off for the blood leaving the implanted internal mammary artery (Fig. 3). The internal mammary artery implant operation has been performed upon hundreds of animals and well over a hundred patients, and it has been shown to remain open up to four years in at least 70% of human cases. The clinical results have been excellent and the senior author has frequently been asked why he proceeded to investigate other operative procedures, and it might be well to answer this question in this article. The



Fig. 5.—Photograph showing ameroid constrictors which have been slipped around the origins of the anterior descending and circumflex branches of the left coronary artery.

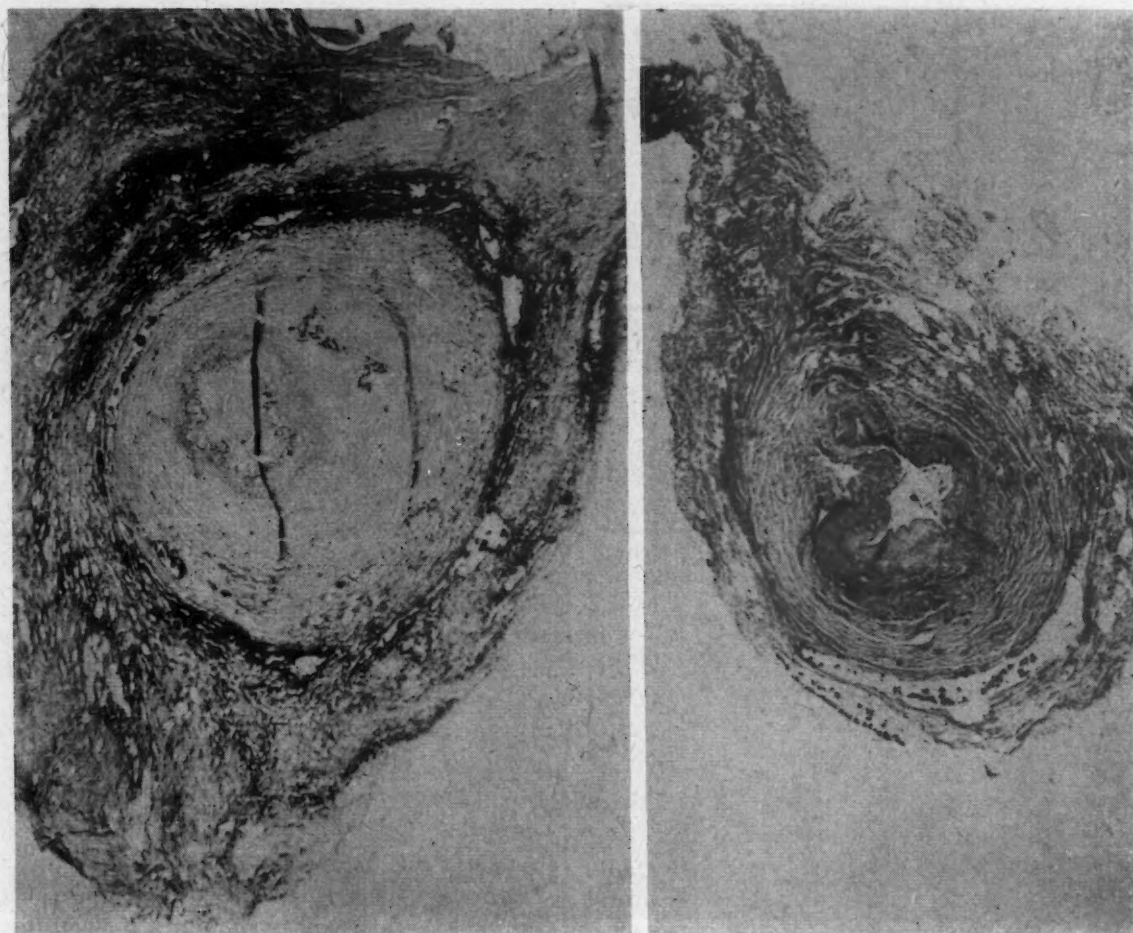


Fig. 6.—Photomicrograph of sections through the site of ameroid constriction of anterior descending and circumflex branches of the left coronary artery.

reason for further searching, which has continued over the past eight years, is that the implanted internal mammary artery, like other transplants elsewhere, carried a danger of subsequent blocking in roughly 20% of cases. Secondly, it has been shown in a human patient who did not get well and was not relieved of his anginal pain after his internal mammary artery implantation, when he died from a rupture of a right ventricular aneurysm, that the only artery open in his heart was the internal mammary artery placed there 3½ years previously. It was quite evident that this one artery was not large enough to supply enough blood to replace the blood which would have been supplied by all three coronary arteries in this heart if they had remained open. The left ventricle appeared to be in the same condition as it was at the time that the internal mammary artery was placed there. In other cases it was quite evident that where there was a very large hypertrophied left ventricle, the size of the internal mammary artery, which is larger than a coronary artery, was not sufficiently great to supply blood required by a hypertrophied left ventricular muscle mass. For this reason a search has been made for other methods of revascularization which could supplement the internal mammary artery implantation procedure. Many operative techniques have been studied, from omentopexy to the Vineberg sponge operation, and these have been tested against the coronary artery

ameroid constriction test.²⁻⁵ This test was developed in 1956, when satisfactory mechanical coronary artery constrictors were devised which could be placed around the origins of coronary arteries. The ameroid constrictors (Fig. 4a, b) are composed of a segment of a plastic rod into which a central lumen communicating with a peripheral slot has been drilled. This plastic material is surrounded by a steel jacket. The plastic absorbs water and in so doing expands in all directions. Peripheral expansion is prevented by the steel jacket, so that the expansion of the ameroid is directed towards narrowing of the central lumen in which lies the coronary artery. The rate of absorption and therefore the rate of expansion can be controlled by coating the ameroid with petrolatum jelly. To reduce experimental error to a minimum, ameroid constrictors are made in batches, mixed up and placed in a desiccator. The size of the lumen is drilled to precision, measuring 110/1000 inch, and is checked by a rod measuring 110/1000 inch, before the ameroid is placed around the coronary arteries. Animals weighing between 40 and 50 lb. are used. Each week a control animal is operated upon, that is, an animal in whom only the ameroid constrictors are placed around the coronary arteries (Fig. 5). When ameroid constrictors are placed around the anterior descending and circumflex coronary arteries of the canine, 85% of the animals die within a 30-day average period. It has been

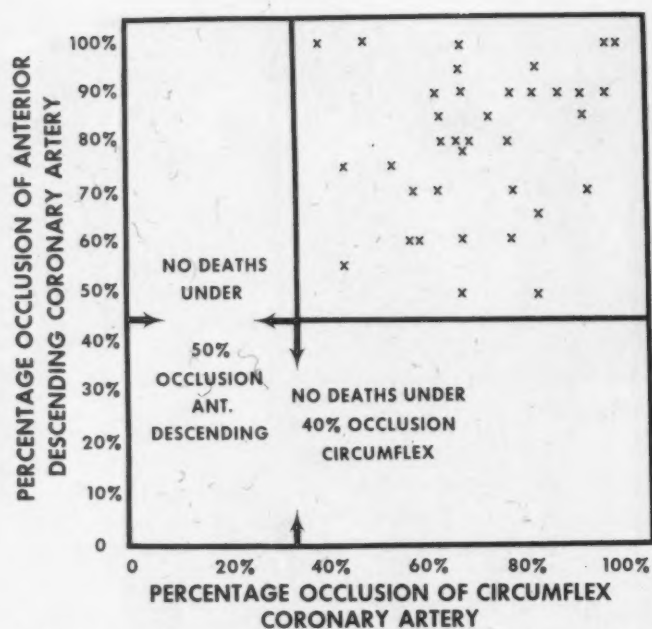


Fig. 7.—Degree of anterior descending and circumflex coronary artery constriction by ameroid sleeves in 36 animals out of 38 that died from myocardial ischemia. This shows the point of critical coronary artery narrowing. Note that animals died when the combined average cross sectional area of the lumina of two major coronary arteries was reduced by 50% or more.

noted that such animals die suddenly while fighting, eating or running, and frequently die without any evidence of myocardial infarction. Further, it has been shown that it is not necessary to have complete occlusion of the lumina of the coronary arteries to cause death (Fig. 6). The animals, like man, reach a point of critical coronary artery narrowing, at which point a sudden demand of the myocardium for blood beyond the points of coronary artery narrowing results in their death. Micro-histological measurements of the coronary arteries in each animal have been made at the point of coronary artery narrowing. It has been found that animals die when the combined cross-sectional area of the two coronary arteries has been reduced by an average of 50% or more (Fig. 7). Many revascularization operations have been tested against coronary artery ameroid constriction death. By that we mean that the ameroids are placed in position on the coronary arteries and then the operative procedure which is claimed to be of value is carried out. The value of an operative procedure is judged by the number of animals that survive ameroid constriction of the origins of the anterior descending and circumflex branches of the left coronary artery, as compared with control animals.

During the course of these searches and studies it became clear that the epicardium and the serous layer of the pericardium presented physical barriers to the entrance of extracardiac blood vessels into the myocardium.

The importance of removing the epicardial barrier was recognized by Beck and Leighninger⁶ in 1934, when they first performed their pectromyopexy. Since that time much attention has been directed by many investigators to removing this barrier to the ingress of blood vessels from the

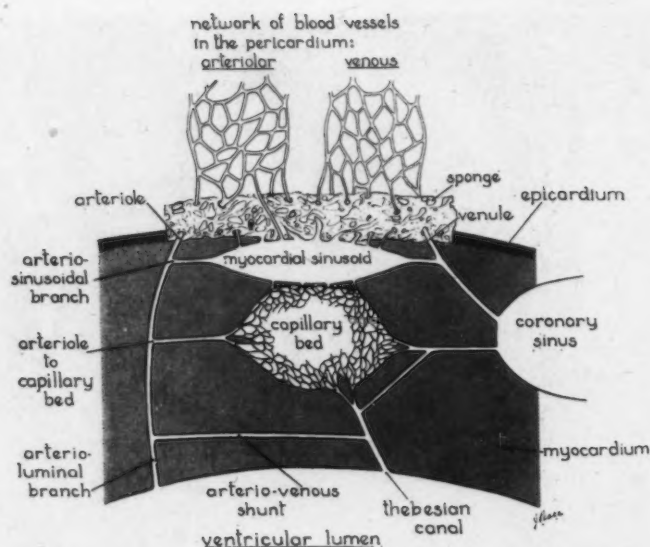


Fig. 8.—Drawing demonstrating Ivalon sponge operation.

pericardium into the myocardium. Numerous methods for removing the epicardium have been devised, ranging from mechanical scraping to the introduction of abrasives, chemicals, etc., into the pericardial sac.

In 1953, removal of the epicardium was carried out, using scissors and special instruments in order to prepare a bed for pericardial fat pads which were sewn directly to the myocardium. This procedure was reported by us,⁷ and it was shown that there was very little reaction between the myocardium and the pericardial fat pads when the latter were laid directly on the myocardium. Following this we developed special techniques for removing the epicardium.

Strangely enough, all efforts have been directed in the past towards removing the epicardium to allow the entrance of blood vessels from the pericardium into the myocardium from extracardiac sources.⁸⁻¹⁰ It had apparently not occurred to others, as it did not occur to us, that removal of the epicardium may considerably alter the hydrostatics of the myocardial circulation which has nothing to do with the ingrowth of new vessels into the heart muscle.

Five years ago, while working with the Ivalon sponge operation, the senior author became aware of the fact that removal of the epicardium resulted in changes within the myocardium.¹¹⁻¹³ In the experimental animal it was clearly evident that the removal of the epicardium and application of a 1/16" Ivalon sponge to the myocardial surface provided a high degree of protection against coronary artery constriction death (Fig. 8).

Many injection studies of the Ivalon-sponge-treated ischemic hearts were made. Definite arteriolar or larger-sized communications were demonstrated between the mediastinal arteries and the myocardial and surface coronary arteries. These were outlined by Schlesinger mass, which does not penetrate arterioles smaller than 30 to 40 microns (Fig. 9a, b, c, d). In addition to these vessels,

Fig. 9a

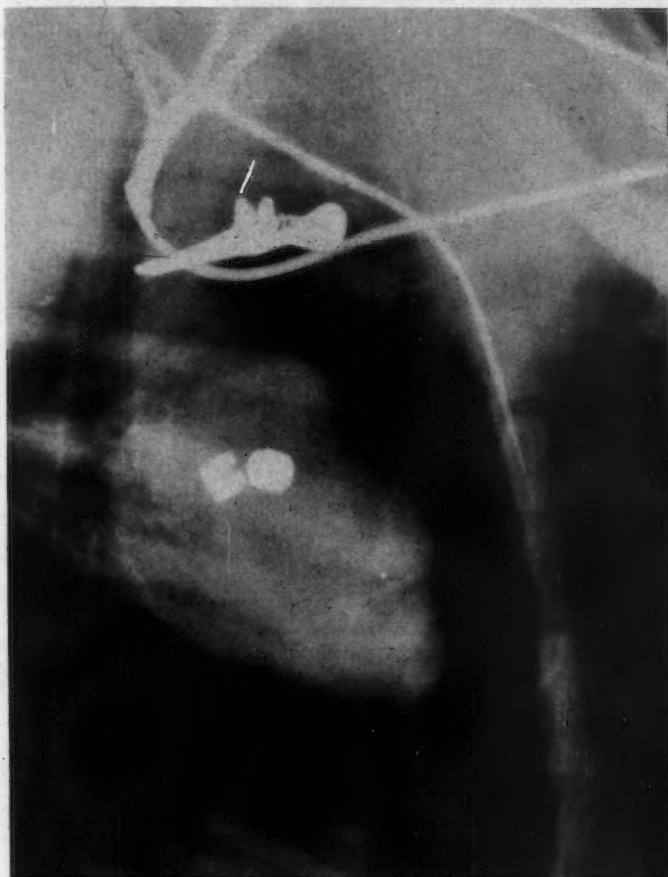


Fig. 9b

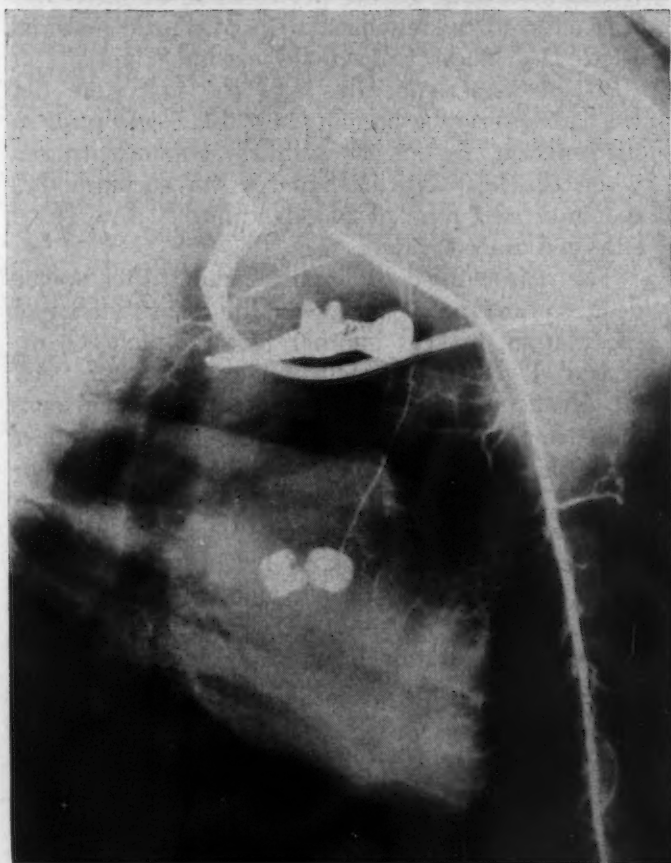


Fig. 9c



Fig. 9d

Fig. 9.—Reproduction of an angiocardiogram made on the heart of an animal 12 months after the Ivalon sponge operation and survival from ameroid constriction of the two major left coronary arteries. The radiopaque dye was injected through the left subclavian artery after first ligating its origin at the aorta. 9a.—Control showing ameroids in position on the anterior descending and circumflex arteries. 9b.—Demonstrates the filling of the numerous branches which originate in the axillary, subclavian and internal mammary arteries to converge in the region of the left ventricle. 9c.—The beginning of opacification on the anterior wall of the left ventricle is defined with faint opacification of the anterior descending branch. 9d.—Clearly defined areas of opacification in the approximate situation of the Ivalon sponge sheets placed on the left ventricle.

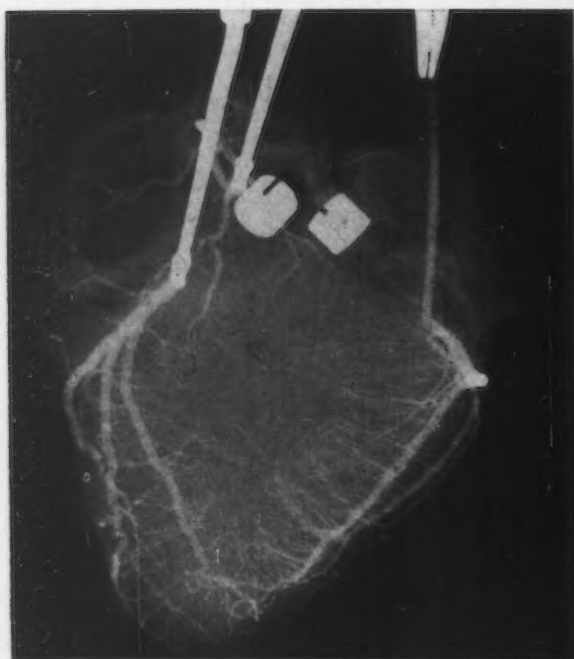


Fig. 10a

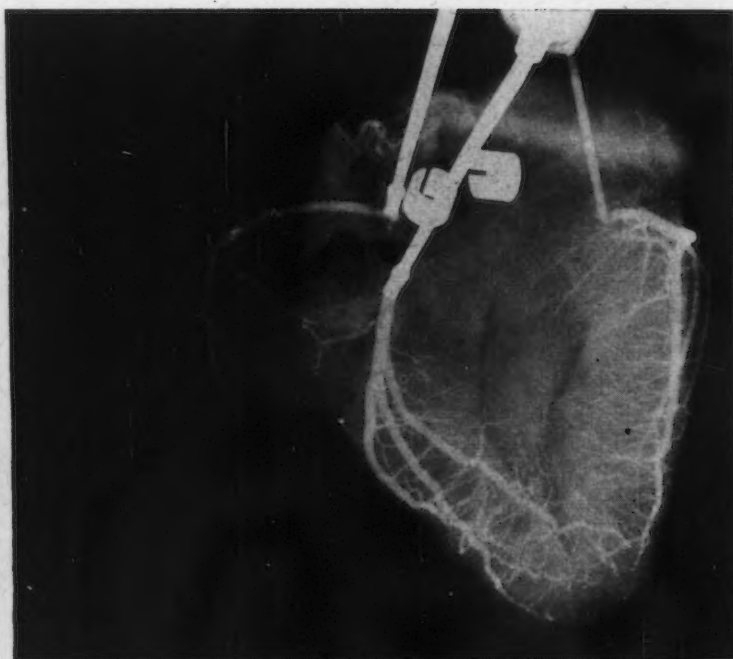


Fig. 10b

Fig. 10—Roentgenogram of Ivalon sponge on heart of animal No. 435 in which the anterior descending and circumflex arteries were injected with Bellman-Frank mass distal to ameroid constriction. The right coronary artery was likewise injected. 10a.—Intact heart showing numerous vessels leaving surface of coronary arteries toward the left ventricular lumen. Note the number of these and their tendency to palisade and form numerous inter-coronary anastomoses. 10b.—The same heart unrolled. Note the absence of the same type of vessels in the right heart which did not receive Ivalon sponge and in the posterior surface of the left heart where the sponge had not been placed.

numerous large vessels were outlined which communicated with the ventricular lumen (Fig. 10a, b). Both appeared to communicate with the blood vessels which had grown into the sponge sheet lying upon the ventricular surface. It was considered that the sponge-treated animals survived ameroid coronary artery constriction because of the ingrowth of the mediastinal vessels through the sponge to reach the myocardium, and that possibly the numerous arterioluminal vessels which were outlined were functional.⁷⁻⁹

In early 1958, this operation was applied to human patients with coronary artery disease who were suffering from chronic heart failure, with enlarged right and left ventricles. Many of these patients, after administration of the anesthetic, required vasopressors and had to be placed in acute Trendelenburg position in order to maintain a blood pressure of 80 mm. Hg. Operation was proceeded with and, much to our surprise, after removal of the epicardium there was marked improvement in cardiac function. This was clearly evident by the increased vigour of cardiac contraction and by the fact that the Trendelenburg position and vasopressors were no longer necessary. It was also noted at the time that cardiac function and blood pressure had improved and that the heart appeared to have grown larger. When this apparent cardiac enlargement was first noticed it was questioned. However, there was little doubt when the time came for pericardial closure. It was found then that closure of the pericardium resulted in a marked drop in blood pressure which immediately returned to previous levels once the pericardial sutures were

released. Closure of the pericardium in such cases was effected by sewing a strip of plastic material, 1" to 1½" wide, to each pericardial edge.

In our experience this was the first time that we had observed a human heart dilate and improve its function, except after mitral commissurotomy when the left ventricle enlarges to accommodate the increased flow of blood admitted through an enlarged mitral valve.

The reason for cardiac enlargement after epicardectomy in such cases was the cause of much speculation, as was another factor which we observed. It was noticed in these desperately sick, far-advanced cases of coronary artery insufficiency that after epicardectomy the blood which oozed from the raw myocardial muscle surface was blue-black. Much to our surprise, inspection of the same area half an hour later showed that it had changed from blue-black to bright red, revealing many punctate areas from which bright red blood oozed.

The source of this bright red blood in beating human hearts in which the total cross sectional area of the main coronary arteries was reduced more than 90% was indeed puzzling. Certainly, the removal of the epicardium could not have altered the lumina of blocked coronary vessels to permit the filling of the myocardial vessels with oxygenated blood.

It was obvious that since these hearts changed colour and improved in function, oxygenated blood must have been introduced from some source other than the blocked coronary arteries. The only possible source of readily available blood

under such circumstances had to be the left ventricular lumen.

In the animal it had been observed that the sponge operation appeared to stimulate the formation of many arterial luminal vessels, and it was postulated that perhaps, after the sponge operation, ischemic hearts received blood both from extracardiac and intracardiac sources, the latter by endocardial nutrition. Since the first stage of the sponge operation is epicardectomy, our attention has been drawn to the epicardial structure in an attempt to explain some of the foregoing facts.

THE EPICARDIUM

There is actually very little known about epicardial structure. A search of the literature, including early century textbooks of anatomy, yields little information. However, in a recent edition of Gould's "Textbook of Pathology"¹⁴ there is a most illuminating description of this structure. The source of Gould's information apparently stemmed from an anatomical confrère.

Gould refers to the pericardium as a two-layered structure, the outer being composed of a thin layer of mesothelium, a simple squamous or cuboidal epithelium; the other, or deeper layer, is composed of fibroelastic connective tissue. The connective tissue layer of the epicardium contains a considerable amount of fat around the sulci and around the layer of vascular channels which lie over the surface of the ventricle. It is continuous with the connective tissue forming the serosa of the great vessels entering and leaving the heart. The deep layer of the epicardial connective tissue is continuous with the perimysium of the myocardium. The perimysium is a dense layer of fibroelastic connective tissue which surrounds groups of muscle fibre bundles.

It is in this layer that one finds a network of blood and lymph capillaries and myocardial sinusoids traversing the full thickness of the epicardium.

FUNCTION OF THE EPICARDIUM

From the structure and distribution of the epicardium it would appear that this very tough fibroelastic structure which completely covers the chambers of the heart and coronary vessels performs a function during the cardiac cycle. This function may be likened to that of the fibroelastic tissue in the lung which helps the lung to contract actively during expiration. In the higher forms of animal life the epicardium is well developed, whereas in the lower forms of life it is poorly developed or completely absent. In the mammalian heart, theoretically, the epicardium should assist systole and to some degree limit the extent of diastole. Its presence is necessary to assist in the rapid filling and emptying of the cardiac chambers. In the higher forms of life, sudden physical effort, such as a hundred-yard sprint, calls for sud-

den increases in cardiac output. The presence of the epicardium covering the heart surface and dipping down, as it does, to surround the bundles of myocardial fibres must contribute to the overall compactness and efficiency of the contracting myocardium.

THEORETICAL EFFECT OF EPICARDIAL REMOVAL

The removal of this tough fibroelastic layer from the surface of the myocardium theoretically should result in overall bulging of the myocardial fibres, much in the same way as a gastrocnemius muscle belly bulges through an incision in its containing fascia. This would explain the apparent increase in size observed by us in our human hearts after epicardectomy and application of an Ivalon sponge sheet. Under such conditions the entire myocardial fibre network is loosened, so that the intrinsic sponge-like character of the myocardium is accentuated. Pre-existing arterioluminal and myocardial sinusoidal spaces enlarge. Further, it could explain part of the results obtained by Beck I operation, because in this operation, as in the Vineberg sponge operation, one of the stages of the operation is epicardectomy.

In order to explain our observations and to test our theory on ventricular luminal feeding, it was decided to test the value of the various elements of the Beck I and Vineberg sponge operations in affording protection against myocardial ischemia caused by ameroid coronary artery constriction. In this test ameroid constrictors are placed around the origins of the anterior descending and circumflex branches of the left coronary artery; this results in the death of 85 to 100% of control animals. Such studies might indicate the effectiveness of a single element of a procedure in protecting against death. Careful injection studies were planned to disclose anatomical channels leading from the left ventricular lumen into its muscular wall, as were studies designed to outline channels reaching the myocardial circulation from mediastinal vessels.

For those not familiar with the operative technique of these two operations, the various elements involved in each operation are listed:

The Beck I operation consists of:

- (1) epicardectomy,
- (2) partial ligation of the coronary sinus,
- (3) introduction of asbestos powder sprinkled over the myocardium,
- (4) suturing of pericardial fat pads to myocardium.

The third element, along with the introduction of talc into the pericardial sac, was tested in our laboratory a few years ago and found to be of no value in protecting a heart against myocardial ischemia caused by ameroid coronary artery constriction and, therefore, this procedure was not rechecked. The effect of the introduction of asbestos into the pericardial cavity is to set up an inflammatory reaction with resultant scar formation.

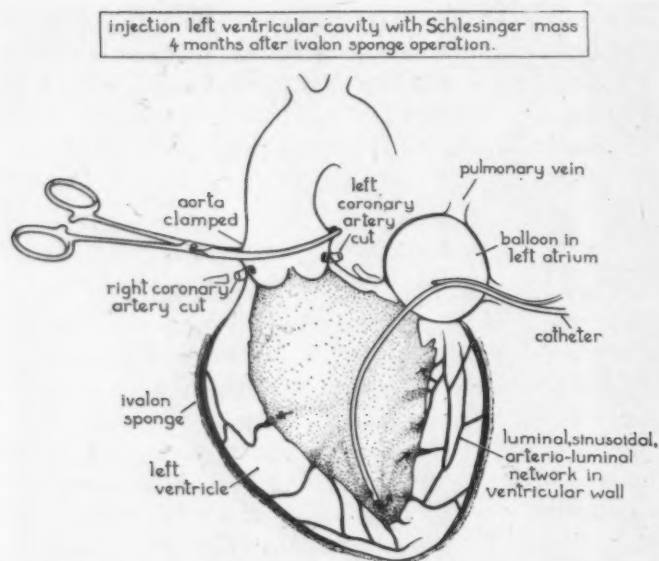


Fig. 11.—Becerra technique of injection of left ventricular lumen in the beating or arrested heart. Note: (1) the cut coronary arteries, (2) the tied aorta and pulmonary veins, (3) catheter in left ventricular lumen introduced through the left atrium via the mitral valve which leads off to a pressure bottle containing the injection mass, (4) Y-connector which permits the beating left ventricle to empty itself before injection or to be siphoned empty if arrested, (5) injections are performed at 100 mm. Hg pressure. This illustration was drawn from a radiograph.

Contracting scar tissue on the surface of the heart quickly negates the value of epicardectomy. The same is true if phenol or other irritants are used for this purpose.

The Vineberg Sponge operation consists of:

- (1) epicardectomy,
- (2) application of a 1/32nd to 1/16th of an inch Ivalon sponge, which is sutured to the bared myocardium,
- (3) removal of the serous layer of the pericardium.

All of these procedures were performed at the same time as the anterior descending and circumflex branches of the left coronary arteries had ameroid constrictors placed around their origins. The rate of survival for each series was recorded and compared with controls in which no procedure was carried out other than placement of ameroid constrictors around the two major left coronary arteries. The degree of occlusion of the coronary arteries was recorded, as was the presence or absence of myocardial infarction.

INJECTION STUDIES

The following injection studies have been carried out:

(1) Left ventricular luminal injection in a beating heart

This type of injection presented many problems, and many techniques were tried and discarded. It was necessary to prevent the injection mass from entering the origins of the coronary arteries if one were to accept the presence of radiopaque dye in myocardial vessels as evidence that it arrived there through ventricular myocardial lum-

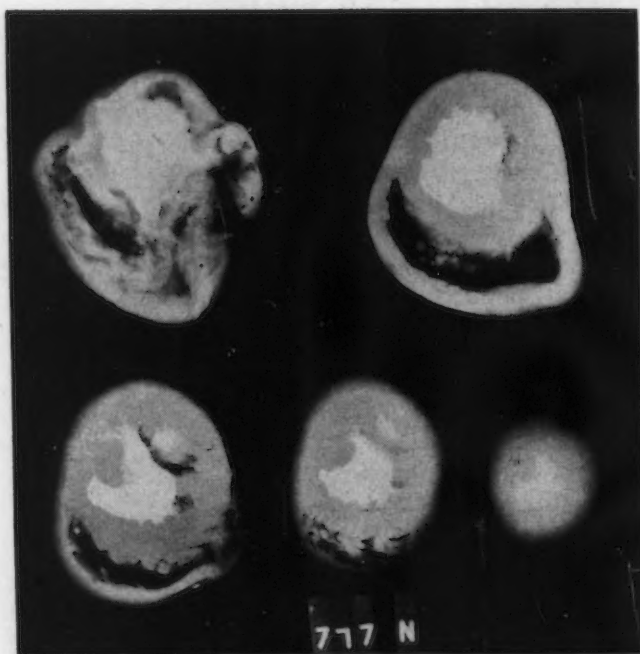


Fig. 12a

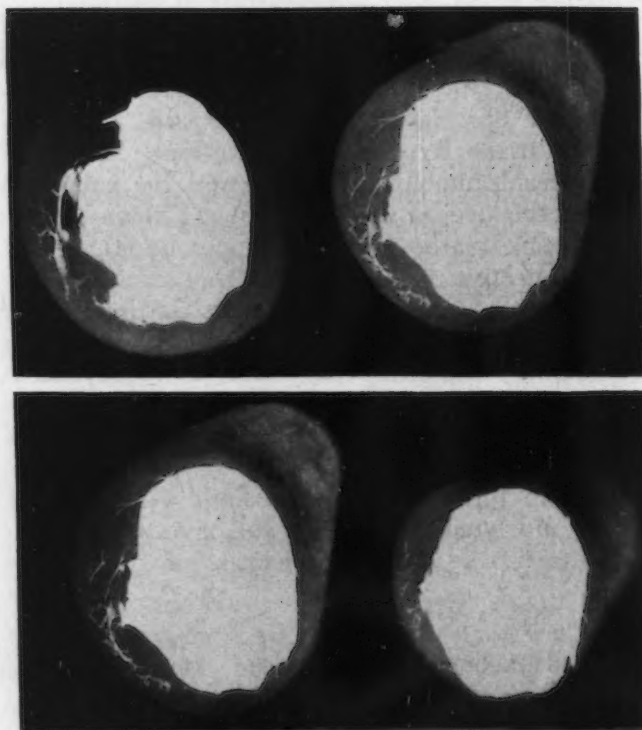


Fig. 12b

Fig. 12.—Injection of left ventricular lumen with Schlesinger mass in beating heart. The heart has been fixed after death and sectioned transversely and then radiographed. 12a.—Roentgenogram of normal heart of animal No. 777. Note the absence of filling of ventricular wall vascular spaces. 12b.—Roentgenogram of heart of animal no. 6 which survived ameroid coronary artery constriction and epicardectomy and was sacrificed five months after operation. Note how the beating left ventricle siphoned the Schlesinger mass into the surface coronary vessels and into its myocardial wall.

inal vessels. Pablo first tried this procedure using a balloon to fill up and to block the outlet of the left ventricle or, in another injection study, to block the mitral valve when the catheter was inserted through the left atrium into the left ventricle. Both of these techniques, although very

ingenious, were found to be inaccurate, as the injection mass could bypass the balloons and enter a septal branch, thereby filling the coronary arteries and leading to a misconception as to the source of filling of the coronary arteries in the ventricular wall.

Becerra has since devised a technique which we now consider to be foolproof.

The Becerra technique of Left Ventricular Injection in the Beating or Dead Heart
(Fig. 11)

(a) A large catheter is inserted into the left atrium through the mitral valve and thence into the left ventricular cavity. The catheter is attached to a bottle containing the injection mass which is kept at a pressure of 100 mm. Hg. A Y-shaped tube is placed in the circuit to allow the beating ventricle to empty itself of blood before the injection is started, or when the heart is not beating, to siphon out blood from the left ventricle before introducing the Schlesinger injection mass.

(b) The pulmonary veins, right and left, are surrounded by ligatures.

(c) The coronary arteries, right and left, are isolated at their take-off from the aorta.

(d) A clamp or heavy tape is placed around the aorta at its exit from the heart, ready to close off the aorta.

The sequence of events thereafter is as follows:

The catheter is threaded through the left atrium into the left ventricle.

The pulmonary veins are tied.

The aorta is clamped, allowing the ventricle to empty itself.

The coronary arteries are ligated at their origins and cut distal to the ligatures.

The injection mass is introduced into the left ventricle.

In this way the left ventricle beats against the pressure of the injection mass column which is not more than 100 mm. Hg.

The coronary arteries are open at their origins, making it possible for the ventricle to siphon the injection mass from the ventricular lumen into the myocardial sinusoidal spaces and anterior luminal vessels into the left ventricle, provided the luminal ventricular spaces are large enough (Fig. 12 a, b).

(2) *Injection of left ventricle in the dead heart*

The injection is carried out with the same sequence as in the injection of a living heart, except that the left ventricle is emptied by suction before the injection mass is introduced.

After the left ventricular injection has been completed in each type of injection, radiographs are taken of the heart and chest *in situ*. The heart is then removed and the radiographs are repeated. The heart is fixed and sectioned transversely, or coronally, and the sections again radiographed.

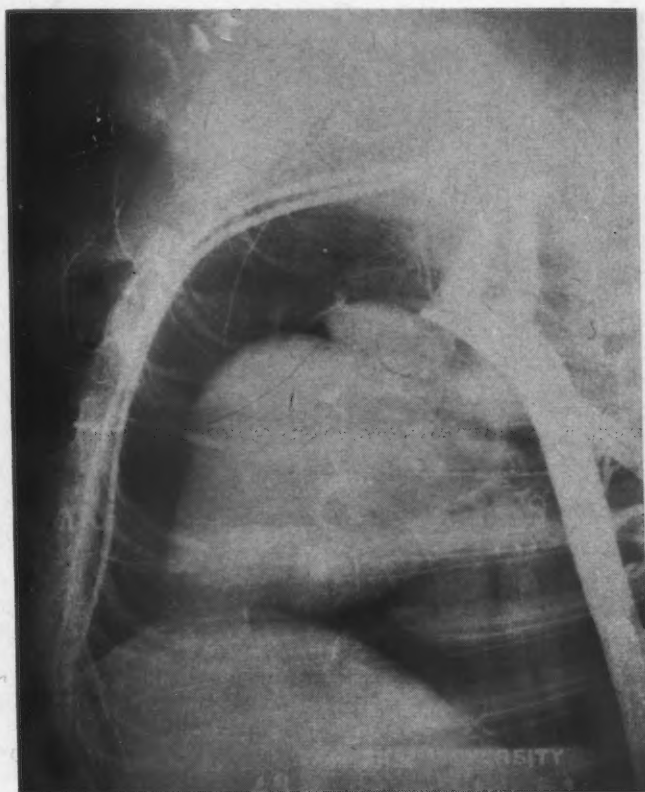


Fig. 13(a).—Injection of thoracic aorta via abdominal aorta with Schlesinger mass. Roentgenogram of normal heart showing no filling of the pericardium or coronary vessels.



Fig. 13(b).—Injection of thoracic aorta via abdominal aorta with Schlesinger mass. Roentgenogram of animal No. 336 that died 30 days after the application of constricting ameroids on the anterior descending and circumflex branches of the left coronary artery. There is no filling of pericardial or coronary vessels following the aortic injection. Similar results have been obtained in animals surviving ameroid coronary artery constriction, partial ligation of the coronary sinus, or in animals surviving coronary artery ameroid constriction and epicardectomy alone.



Fig. 13(c).—Injection of thoracic aorta via abdominal aorta with Schlesinger mass. Roentgenogram of animal surviving coronary artery ameroid constriction in the Vineberg sponge operation, showing the injection mass filling coronary arteries via mediastinal vessels.

(3) Injection of Thoracic Aorta to outline Mediastinal Vessels

The aorta is cut distal to the heart and the distal end is tied. Vessels to the head and proximal limbs are tied off. The injection cannula is inserted into the thoracic aorta via the abdominal aorta below the diaphragm. The injection is made *in situ* so that the injection mass fills the thoracic aorta without entering the coronary arteries. Schlesinger mass is used in all of these injections. This medium will not enter arterioles or vessels of less than 30-40 microns in size. In this way



Fig. 13(d1).—Roentgenogram of left ventricular injection with Schlesinger mass in animal No. 482 which survived coronary artery constriction and Ivalon sponge operation. This animal was sacrificed 22 months after operation.



Fig. 13(d2).—Injection of thoracic aorta via abdominal aorta with Schlesinger mass. Injection of aorta in same animal with Schlesinger mass. Note how the mediastinal vessels have filled and joined vessels in the heart wall.

vessels of this size or larger may be outlined if they are present, leading from the aorta through the mediastinum into the heart. This type of injection has also been made after left ventricular injection in order to try to follow mediastinal vessels into the myocardium to see if they join the luminal ventricular vessels (Fig. 13a, b, c, d1 and d2).

(4) Injection of Coronary Arteries *in situ*

This is a most interesting injection technique. The thoracic aorta is opened just above the aortic valve and the coronary arteries are cannulated. A cannula is introduced into the left ventricle to collect any dye which enters the lumen. Schlesinger mass is used, and the presence or absence of communications between the coronary arterial tree and the left ventricular lumen is noted, as is the filling or lack of filling of the mediastinal vessels. By this technique it is possible to outline all communications between the coronary arterial tree, myocardial spaces and ventricular lumen, as well as communications from mediastinal vessels through the pericardium.

OPERATIVE PROCEDURES

I. Control Studies

Of 27 animals in which ameroids were placed around the anterior descending and circumflex branch of the left coronary arteries, 22 (80%) died after an average period of 19 days, and 5 (20%) lived for three months.

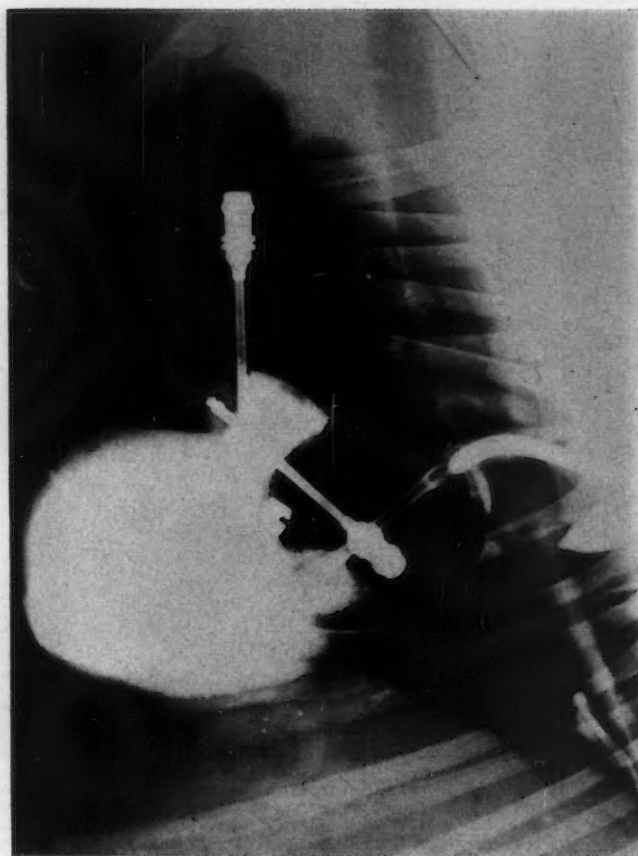


Fig. 14.—Studies of the heart of animal No. 169 which survived coronary artery ameroid constriction and partial ligation of the coronary sinus. This animal was sacrificed four months after surgery. The roentgenogram shows the injection of the left ventricular lumen with Schlesinger mass. Note the absence of luminal myocardial spaces communicating with surface coronary arteries.

Of the 22 animals that died, aortic and coronary artery injection of Schlesinger mass was performed in 10 animals, and in none was there demonstrated any evidence of communications between the left ventricular lumen or mediastinal vessels within the coronary arterial tree (see Fig. 12). Of the five animals surviving, three had aortic injections alone, and in one, coronary arterial filling was seen to occur via adhesions at the apex. Two animals had left ventricular injections of the dead heart, one of which showed subepicardial filling by the injection mass.

II. Partial Ligation of Coronary Sinus Plus Application of Ameroid Constrictors

Of seven animals subjected to this procedure, four (57%) died after an average of 25 days. Three (43%) survived and were sacrificed after 3½ months. All seven animals had left ventricular injections followed by aortic injections. In no heart was there any filling of the left ventricular vessels from the ventricular lumen or from the mediastinal vessels (Fig. 14). There were a few myocardial spaces filled from the lumen of the left ventricle which penetrated the inner one-third of the ventricular wall, which were taken to be thebesian veins.

In all hearts there was a marked increase in inter-coronary vessels.

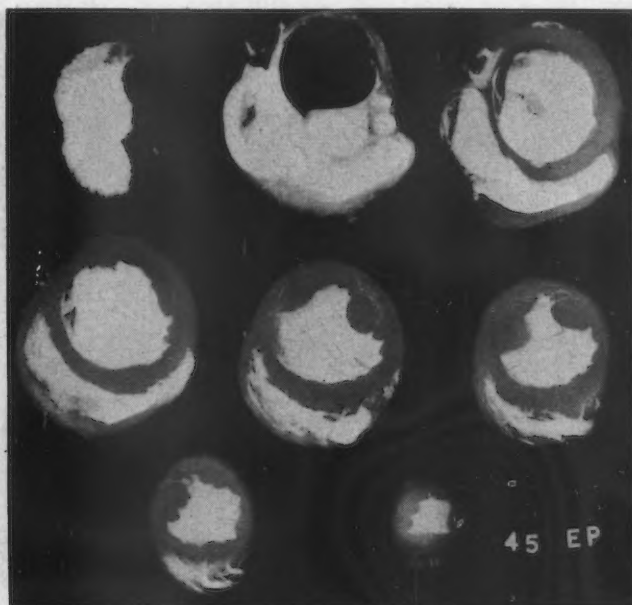


Fig. 15a

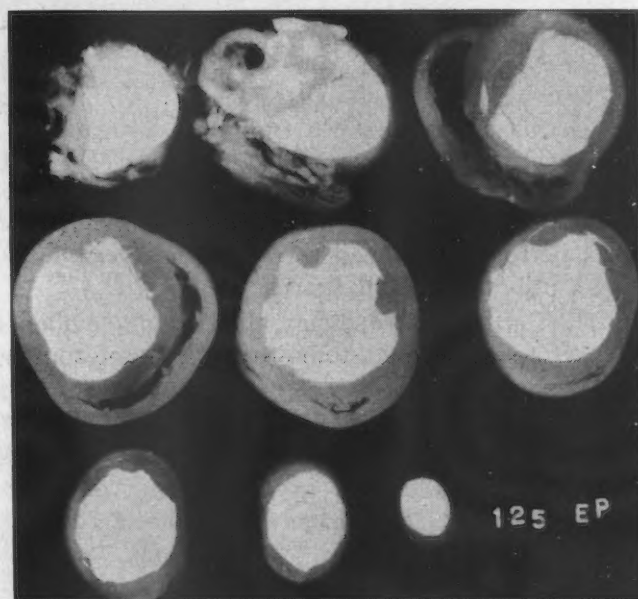


Fig. 15b

Fig. 15.—Epicardectomy and ameroid artery constrictors. (a) Roentgenogram of ventricular injection with Schlesinger mass in a beating heart in animal No. 45 in which the coronary arteries were cut. The study was carried on five months after operation. Note how the Schlesinger mass has been siphoned from the ventricular lumen directly into the ventricular vessels and from the surface coronary arteries. The roentgenogram which is displayed is of a transverse section of the heart. (b) Roentgenogram of heart of animal No. 125 after left ventricular injection with Schlesinger mass in a dead heart eight months postoperatively. The study shows Schlesinger mass filling the arterial luminal and myocardial sinusoidal spaces. It should be noted that the injection was made from the left ventricular lumen only.

III. Epicardectomy Plus Application of Ameroid Constrictors

In the combined series of Becerra and Chari, 17 animals were subjected to this procedure. Of these, seven (41%) died and 10 (59%) survived. Injection of the aorta in nine animals failed to show any filling of the myocardial or coronary vessels.

Injection of the left ventricle in the living, beating heart was performed by Becerra on four animals which survived five months following

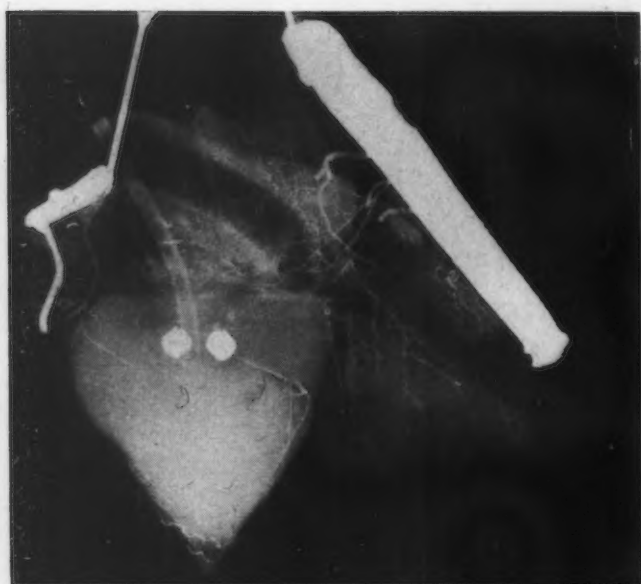


Fig. 16(a).—Epicardectomy, plus Ivalon sponge 1/16", plus removal of serosal layer of pericardium. Roentgenogram of animal No. 150 sacrificed and injection made of the aorta with Schlesinger mass. Note the filling of coronary artery via the aorta, mediastinal vessels, pericardium, and sponge.

epicardectomy and application of the ameroid constrictors. In all four animals the Schlesinger mass was siphoned into the left ventricular wall to fill surface coronary arteries (Fig. 15a). Postmortem injection of the left ventricle in the hearts of two animals sacrificed five months after operation was performed showed arterioluminal vessels and myocardial sinusoidal spaces (Fig. 15b).

Thus, after epicardectomy, there was no evidence of extracoronary anastomoses to account for the high survival rate after ameroid coronary artery constriction. There was, however, evidence that the beating left ventricle siphoned Schlesinger mass

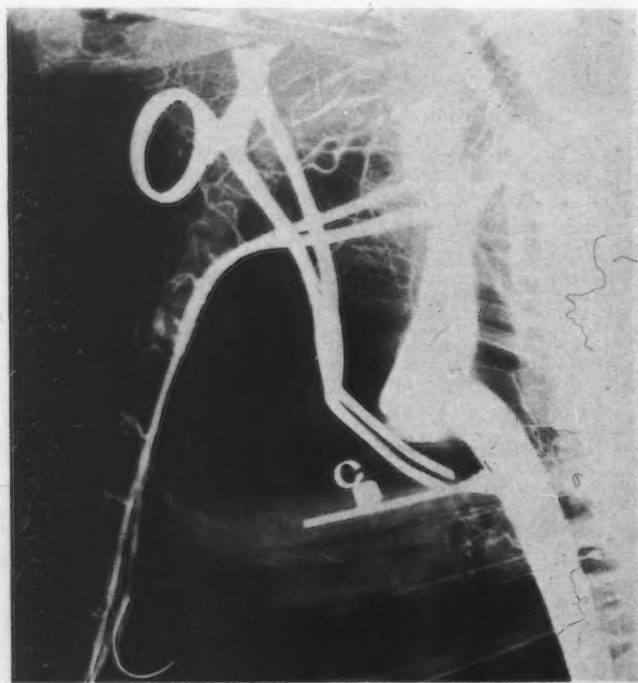


Fig. 16(b1).—Epicardectomy, plus Ivalon sponge 1/16", plus removal of serosal layer of pericardium. Roentgenogram of animal No. 417 after aortic injection of Schlesinger mass showing mass traversing pericardial vessels to join vessels in the heart.

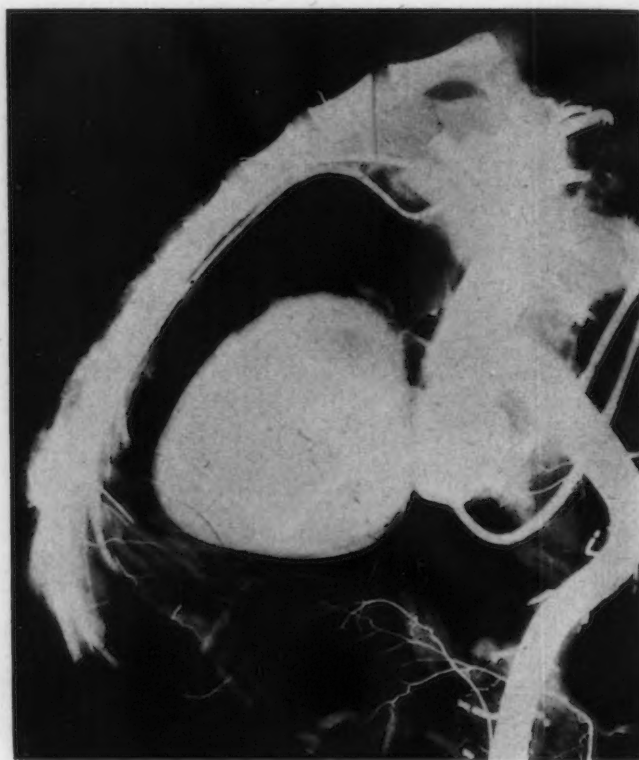


Fig. 16(b2).—Epicardectomy, plus Ivalon sponge 1/16", plus removal of serosal layer of pericardium. Roentgenogram of same animal in which Schlesinger mass has been injected into the left ventricular lumen. Note filling of vessels in ventricular wall and surface.

into the vascular spaces within the left ventricular wall.

IV. Epicardectomy Plus Ivalon Sponge (1/16th Inch) Plus Removal of Serosal Layer of Pericardium

Seven animals were subjected to these operative procedures; none died and all survived 17 months or more.

One of these animals was injected through the aorta only and showed filling of the coronary arteries (Fig. 16a). One animal had an aortic injection which filled the mediastinal vessels and the coronary vessels (Fig. 16 b1). In this same animal the left ventricle was subsequently injected and the Schlesinger mass was seen to join with the vessels in the heart and in the mediastinum (Fig. 16 b2). These injections were made by using Schlesinger mass of two different colours, so that it was possible to follow the course of each injection mass. Three animals had left ventricular injection alone and in these the injection mass entered the left ventricular wall to fill subepicardial vessels, coronary surface vessels and mediastinal vessels (Fig. 16c). Two animals had coronary artery injections *in situ*, in which the injection mass filled the myocardial spaces and entered the ventricular lumen in large quantities. The injection mass also flowed out into the mediastinal vessels to fill the intercostals and the aorta (Fig. 16d).



Fig. 16(c).—Epicardectomy, plus Ivalon sponge 1/16", plus removal of serosal layer of pericardium. Roentgenogram of animal No. 432 in which left ventricular injection was made with Schlesinger mass 22 months postoperatively in dead heart showing injection mass in vessels of the left ventricular myocardium.

SUMMARY OF INJECTION STUDIES

Aortic injection studies of Schlesinger mass have failed to show anastomotic channels of arteriolar or larger size between the mediastinal vessels and the coronary myocardial circulation in: (1) normal animals; (2) animal hearts made ischemic by application of coronary artery ameroid constrictors to the anterior descending and circumflex vessels; (3) epicardectomized animals whose hearts had been made ischemic by ameroid coronary artery constrictors; or (4) animals with partial ligation of the coronary sinus, whose hearts had been made ischemic by ameroid coronary artery constrictors.

Aortic or subclavian injection has filled the coronary arteries via mediastinal vessels after the Vineberg sponge operation in the ischemic heart (i.e. after epicardectomy, followed by the application of Ivalon sponge to the bared myocardium, removal of serous layer of pericardium, and application of ameroid coronary constrictors). The injection mass has also been found within the spaces of the sponge, indicating that blood vessels had grown through the sponge to reach myocardial vascular spaces.

LEFT VENTRICULAR 'LUMINAL INJECTIONS'

(a) Of the living, beating, normal heart.

In a large series of animals a radiopaque substance of the consistency of blood was injected into the left ventricle, and in one out of 10 normal animals the dye was siphoned into the left ventricular wall via the cardiac apex when the coronary arteries were severed, according to the Becerra technique. The left ventricular injection

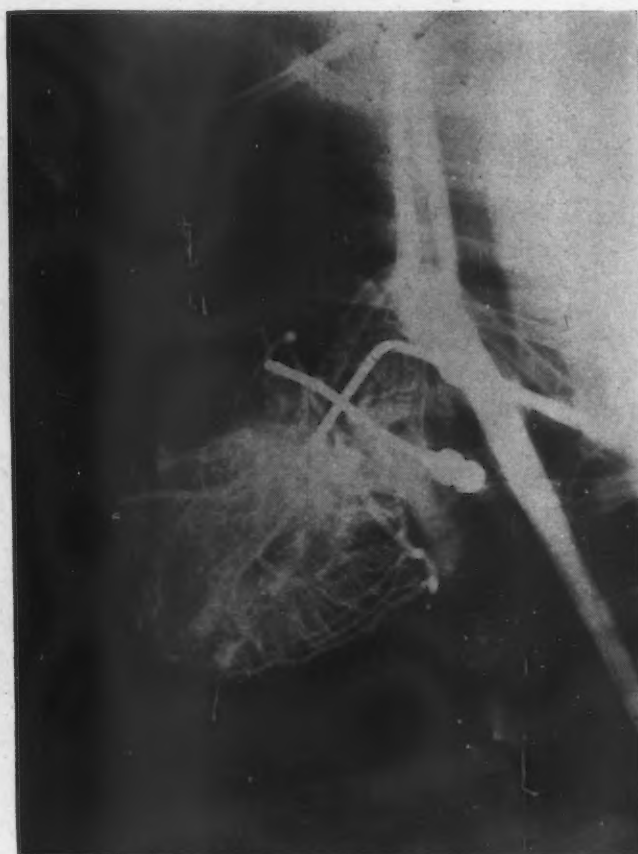


Fig. 16(d).—Epicardectomy, plus Ivalon sponge 1/16", plus removal of serosal layer of pericardium. Roentgenogram of heart of animal No. 445, 22 months post-sponge operation in which coronary arteries were injected *in situ* with Schlesinger mass. Note how the mass filled coronary arteries, then the left ventricular lumen, and out into the mediastinal vessels. In this animal, as in others, the aorta and other mediastinal vessels were filled with Schlesinger mass following injection of the coronary arteries at their origins in the aorta.

was repeated in a series of normal animals, using the Schlesinger mass, and in no animal was there any evidence that the dye, introduced into the left ventricular lumen in the beating heart, was siphoned into the ventricular wall. It was thus seen that some normal hearts are still capable of reverting to luminal ventricular feeding in the region of the apex using channels which are smaller than arterioles, whereas after epicardectomy alone in the presence of narrowed coronary arteries, Schlesinger mass is very definitely siphoned up into coronary and myocardial vessels through the wall of the left ventricle in the beating heart.

(b) Of the dead heart.

Injection of Schlesinger mass into the left ventricular lumen of dead hearts of previously normal animals failed to fill the coronary vessels, whereas in the epicardectomized animals with Ivalon sponge applied to the heart, injection studies showed filling of the myocardial vessels, indicating the presence of numerous luminal-myocardial vascular spaces.

CORONARY ARTERY INJECTIONS *in situ*

The injection of coronary arteries *in situ* in normal hearts and control, artery-constricted ischemic hearts, fails to outline vessels going into the left ventricular lumen or into the mediastinum when Schlesinger mass is used. However, a similar injection into epicardectomized hearts, made

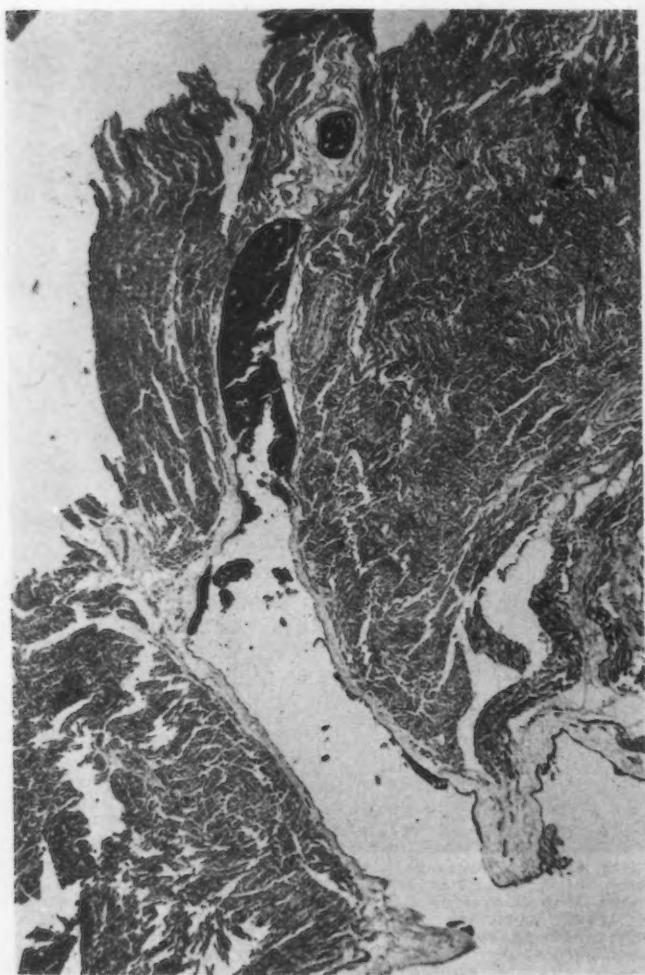


Fig. 17(a).—Photomicrograph of section of heart of animal No. 432 shown in Fig. 16c, showing Schlesinger mass entering a common pathway from the left ventricular lumen.

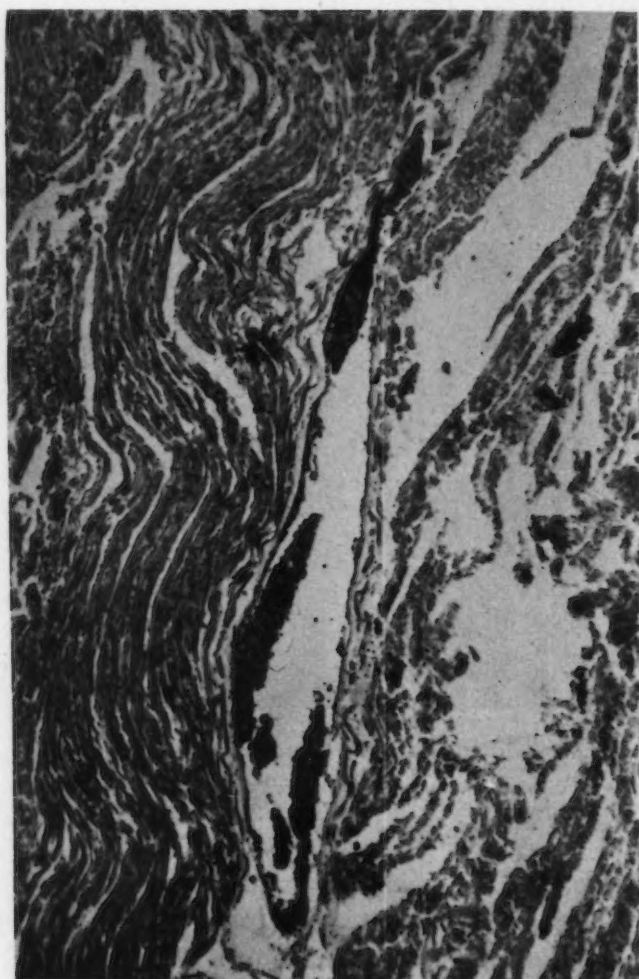


Fig. 17(b).—Photomicrograph of the same heart, showing the Schlesinger mass in the myocardial sinusoids lying between muscle bundles, which has entered via a common ventricular luminal opening.

ischemic, reveals the presence of large vessels communicating with the left ventricle but none with the mediastinal vessels.

Following the Vineberg sponge operation, hearts thus injected show large vessels which penetrate through the sponge out into the mediastinal vessels.

Thus of the elements of the Beck I operation only one, namely epicardectomy, afforded protection from constriction of the two left main coronary arteries. The value of this procedure, we think, is negated when asbestos fibres are spread over the bared myocardium. With each succeeding month the resultant scar formation on the surface of the heart probably returns it to the condition present before removal of the epicardium.

Partial ligation of the coronary sinus failed to open up left ventricular channels and has provided no protection, since all this procedure does is to distribute the blood more evenly within the left ventricle.

The Vineberg sponge operation, on the other hand, opens up large luminal ventricular channels which are probably kept open by the sponge network intimately associated with the surface of the heart, and it further allows the growth into the interstices and thence into the myocardium of many vessels from the mediastinum.

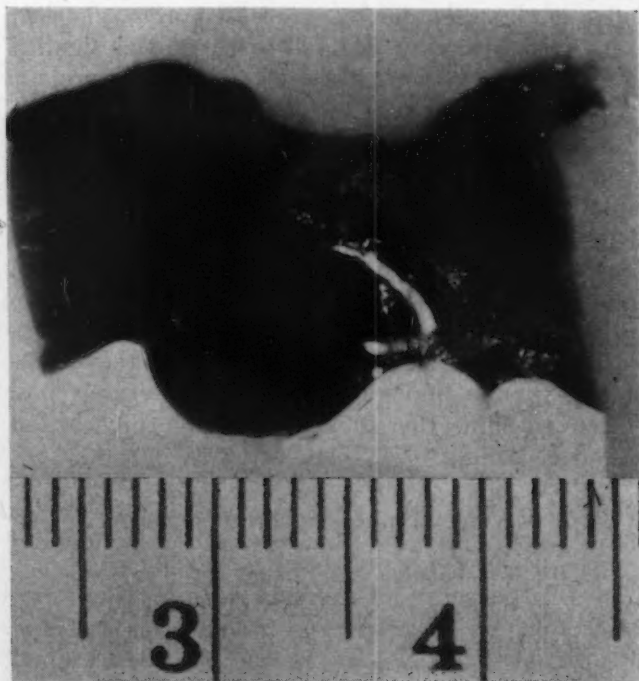


Fig. 17(c).—Photograph of block section taken through animal's heart in which there was a successful left ventricular luminal injection with Schlesinger mass. The white areas are vascular channels filled with Schlesinger mass. Note how the large $\frac{1}{4}$ " vascular channel arises from the left ventricular lumen to divide in the myocardial wall.

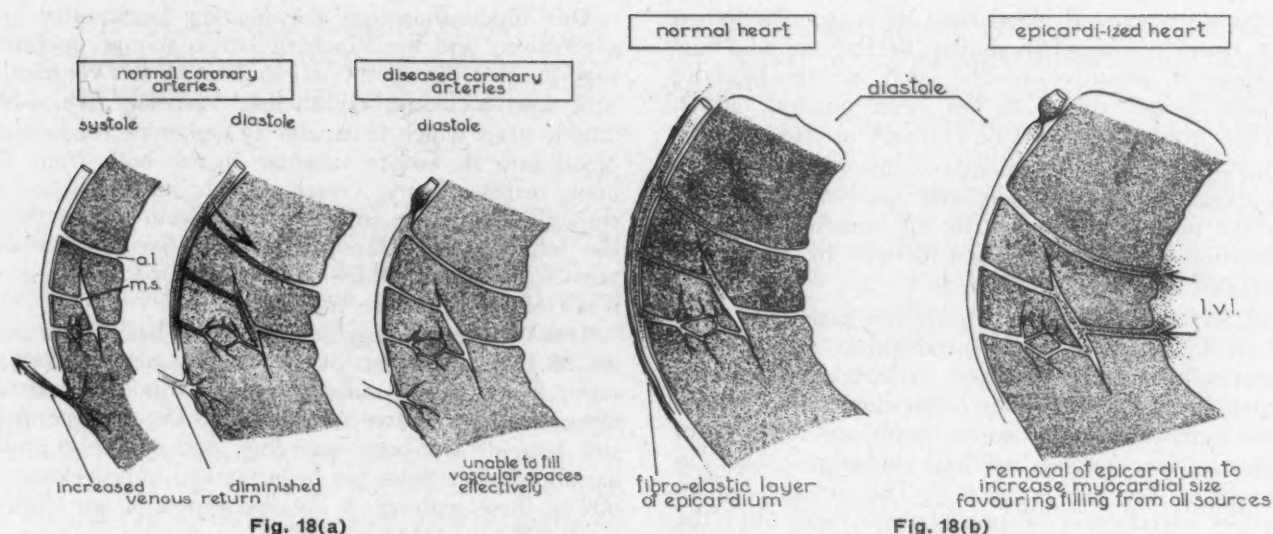


Fig. 18(a).—Diagram showing the effect of coronary artery occlusion on myocardial hydrostatics. The vascular spaces in the myocardium are not effectively filled during diastole when the coronary arteries are narrowed or occluded. (b).—The effect of epicardectomy on myocardial hydrostatics. There is an apparent increase in heart size following epicardectomy with resultant enlargement of myocardial vascular spaces. In the presence of narrowed or occluded coronary vessels this favours inflow from the ventricular cavity into the heart wall. The Ivalon sponge tends to keep the heart in its enlarged state after epicardectomy and encourages the formation of many more luminal ventricular wall vessels.

CONCLUSIONS

Evidence has been presented which, it is believed, indicates that the hydrostatics of the myocardial circulation can be definitely altered under certain conditions. It has been shown that in the presence of occluded or narrowed left coronary vessels, the removal of the epicardium over the entire left ventricle results in the opening up of primitive, previously present, at least 400-million-year-old channels, described by Wearn and confirmed by us in many other studies. These channels run between the coronary arteries and the vascular spaces between muscle fibre bundles known as the myocardial sinusoidal spaces; and between the myocardial sinusoidal spaces and the ventricular lumen itself. In the very early vertebrates there were no coronary arteries. The ventricular myocardial fibres were nourished directly from the ventricular lumen by an ebb-and-flow mechanism. During the evolutionary process and with the development of coronary arteries these primitive channels running from the ventricular lumen into the wall of the ventricle were used less and less. However, there is an animal swimming in the depths of the South Pacific whose paleolithic age is at least 400 million years and whose systemic heart has no coronary arteries and no nerves. Its heart muscle receives nutrition entirely from the ventricular lumen. This primitive creature is popularly known as the "hagfish."

In the presence of narrowed coronary vessels the blood, during diastole, does not enter these spaces as freely and thus encourages the empty spaces to siphon up oxygenated blood from the left ventricular lumen.

When Ivalon sponge is placed on the denuded myocardium it is our opinion that it encourages blood vessels to grow through from the pericardium and perhaps maintain the heart in its enlarged state following epicardectomy. Certainly, in animals observed for as long as 17 months after application of Ivalon sponge to the myocardium, the lumina of ventricular vascular spaces are very large, some of them almost the size of small coronary vessels (Fig. 17).

Our concept of the hydrostatics of the myocardial circulation in the presence of narrowed or occluded coronary arteries, and in the absence of the epicardium, might be presented as follows:

During systole the blood is squeezed from the myocardial vascular spaces out into the venous drainage system. During diastole, owing to the narrowed coronary vessels, blood cannot fill the empty vascular spaces (Fig. 18a). After epicardectomy the heart enlarges, as do the vascular spaces in contact with the ventricular cavity, permitting blood to enter the heart wall (Fig. 18b). Thus the ventricular myocardial network, in communication with the ventricular lumen, acts in the same way as a bathroom sponge, and by surface tension continuity siphons the blood from the left ventricular lumen to fill its empty vascular spaces. By this technique, therefore, the heart is capable of

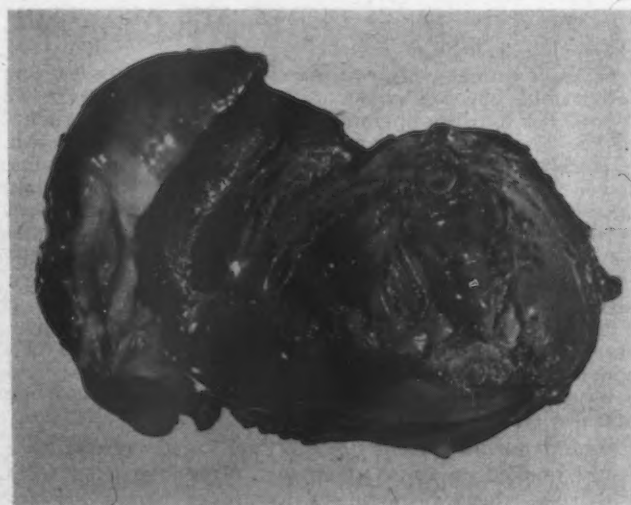


Fig. 19.—Heart of dog 27 days after implantation of arterial graft with polyethylene tubing attached. The left ventricular wall has been cut open to show the open end of the polyethylene tube lying on the surface of the left ventricle (bottom left). Note that the lumen is free of thrombi. The artery attached to this tube was completely patent. However, injection with Schlesinger mass failed to show any evidence of branching of the graft.

obtaining oxygenated blood from its ventricular lumen in a manner somewhat similar to the ebb-and-flow nutrition of primitive hearts, such as the hagfish's systemic heart which, as has been pointed out in previous publications, has no coronary arteries.

Our clinical and experimental evidence now supports this thesis. To have endocardial nutrition, therefore, it is not necessary to postulate an isometric phase of contraction—which has been denied by some and postulated by others.

In 1951 and 1952, working on the basis that there was an isometric phase of contraction in which it was theoretically possible for blood to leave the left ventricular lumen to enter the ventricular wall, experiments were carried out by the senior author to form what was then termed "artificial thebesian canals" in the wall of the left ventricle.¹⁵ This project, which included introduction of polyethylene tubes into the ventricular lumen, leaving one end open in the lumen and the other end in the myocardium, along with similar attempts using free arterial grafts and combinations of grafts with polyethylene tubes, was abandoned when most of these artificially created canals were blocked. However, some of them did remain open, and it is interesting to reproduce an illustration of the inside of the left ventricle showing the polyethylene flanged tube which remained open and through which Schlesinger mass entered the ventricular wall after injection into the tube (Fig. 19). In these animals no attempt was made to create ischemia, and unquestionably this was a factor in the closure of the channels which we were attempting to create between the left ventricular lumen and the myocardial muscle wall.

Our observations on the beating heart after epicardectomy and the Vineberg Ivalon sponge operation suggests that the operation converts the left ventricular wall into a living, contracting vascular sponge-like muscle mass which is capable of siphoning oxygenated blood into its empty vascular spaces both from the many extracoronary vessels which have reached it through the sponge interstices and from the cavity of the left ventricle through the primitive 400-million-year-old channels which have been opened up as a result of the operative procedure.

The Vineberg sponge operation has been performed on 26 human patients with coronary artery insufficiency, 22 of whom suffered from chronic ventricular failure. The operative mortality for these desperately sick patients has been very low, and follow-up study has shown that there has been marked improvement in 80% of these patients. A detailed report of our clinical results is now being compiled.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Given a patient with a displaced uterus which is causing her trouble, however, what are we to do for her? Are we to rush her into the operating room, and, by some brilliant method of surgery, attempt to restore the woman to health, or are we to endeavour to attain the same object by some slower, but safer, procedure? The answer will depend altogether upon the nature of the case and the circumstances and surroundings of the patient. Women who come under our care in the wards of a public hospital seldom have the time to spare from their household duties to permit of their taking a long rest in bed, together with a protracted course of massage and local treatment of the pelvic organs, and, therefore, they require more drastic handling than their more fortunate sisters, but the knife should always be held in the background until all other means of help have been carefully considered.

Anterior displacements of the fundus are rarely sufficiently marked to cause symptoms, other than that form of dysmenorrhoea beginning a few hours before the appearance of the flow and ceasing, or at all events becoming greatly lessened, after the flow has once been fairly established. This class of displacement will almost invariably yield most satisfactory results to a thorough dilatation of the cervical canal and curettage, followed by the stitching in place of a tube inserted into that passage and left there

for from twelve to fourteen days, by which time the slight lacerations which have been caused in the muscles of the sphincter at the internal os will have been pretty well healed. The procedure removes any diseased mucous membrane which may be present and straightens the uterine canal, thus allowing of much better drainage than existed previous to this manipulation. The first menstruation succeeding the operation is apt to be painful, of which fact the patient should be warned, but the future periods will usually be free and painless for some years to come, and even for all time if the patient becomes pregnant and gives birth to a full term child.

Very occasionally, the anteverted uterus will be found to press upon the bladder, causing irritability of that viscus. Here the efforts of the physician should be directed towards improving the various muscular structures which hold the uterus in its usual position. This may be effected by the exhibition of tonics, such as iron, arsenic, strychnine, etc., together with general massage, Swedish movements, and local treatment by electricity, tampons, douching, etc. The application of a well-fitting cradle pessary is at times found useful, sometimes allowing pregnancy to occur, which may be followed by cure, owing to the changes produced during involution.—F. A. L. Lockhart, *Canad. M. A. J.*, 1: 1047, 1911.

CLINICAL AND LABORATORY EXPERIENCES WITH A NEW INTRAVENOUS TETRACYCLINE DERIVATIVE*

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D. DANA, M.D.,‡ Toronto

A NEW synthetic tetracycline (Reverin,[®] Hoechst Pharmaceuticals of Canada, Ltd.) has become available by the addition of a pyrrolidinomethyl chain to the tetracycline nucleus. This new combination is extremely soluble in water and is almost free of any side effects when injected intravenously. Other interesting features, particularly the high blood and urinary levels attained, will be reviewed hereinafter in detail.

METHOD

Extensive bacteriological investigations by Dimmling *et al.*¹⁰ have shown that the potency and the bacteriostatic range of pyrrolidinomethyl tetracycline (Reverin) correspond exactly to that of tetracycline hydrochloride.^{4, 9, 10}

We began by repeating some of this work and our findings follow. When tested against freshly isolated pathogens the minimum inhibiting concentration of antibiotic (M.I.C.) was determined. A concentration of 0.16 to 1.6 $\mu\text{g./ml.}$ is therapeutically effective against sensitive Gram-positive cocci. A concentration of 1.31 $\mu\text{g./ml.}$ is sufficient to inhibit all examined streptococci and at least 65% of tested staphylococci and enterococci.

1. Assay

The medium selected was "Antibiotic Assay Broth" BBL, No. 01-171, adjusted to pH 7.6 when necessary.

An antibiotic working solution (Reverin) of 360 $\mu\text{g./ml.}$ was prepared.

A variety of organisms were tested for sensitivity by serial dilutions with the above-described antibiotic working solution.

These test organisms were cultured in the selected media and diluted with the selected media to approximately a concentration of 9000 organisms/ml. by means of the McFarlane nephelometer method.

From these a strain of *Staphylococcus albus* was found to be consistently sensitive to 0.18 $\mu\text{g./ml.}$ of the antibiotic (i.e. the growth of the test strain was inhibited in tube No. 12, therefore giving tube No. 12 a concentration of 360 $\mu\text{g./ml.}$ of antibiotic with this test strain.)

In order to assess the blood levels obtainable, 10 control patients free of any infections were

studied. These included subjects with hypothyroidism, hypertension, herniated intervertebral disc and hemorrhoids. The blood and urine of each test patient in all cases were tested for inhibitory action on the bacterial test strain. This was taken into account in the evaluation of results. Sterile precautions were taken throughout in all phases of the investigation. Each patient was given a single dose of 275 mg. of pyrrolidinomethyl tetracycline (Reverin), equivalent to 250 mg. of pure tetracycline, intravenously. The preparation was dissolved in 10 c.c. of distilled water and the injection was administered slowly, lasting a full minute. At this time, zero hour, each patient's bladder was emptied completely and the urine was discarded.

At 02.00, 04.00, 08.00 and at 24.00 hours, the bladder of each patient was completely emptied by catheter and each urine sample was collected separately for determination of the antibiotic content. The pH was adjusted to 7.6, using citric acid if alkaline, and disodium phosphate if acid. Blood samples were also collected by sterile technique from each test patient at the same time intervals.

Each urine and blood sample was serially diluted through 12 tubes, using the selected media, and a constant volume of the diluted bacterial test strain (conc. of 9000 organisms/ml.) was added. The dilutions were then incubated at 37° C. for 12-18 hours and read. The last tube in which the growth of the test organism was inhibited was thus taken as the approximate "end point", i.e. if the "end point" was reached at tube No. 6, the concentration equalled 5.63 $\mu\text{g./ml.}$ of antibiotic.

To determine a more accurate level of concentration of the antibiotic, further series of dilutions were carried out between the "end point" obtained and the next lower dilution, thus determining the intermediate values.

The results of all tests were recorded, averaged and plotted on a graph.

	2 hours	4 hours	8 hours	24 hours
Blood level	4.22	2.56	1.43	0.32
in $\mu\text{g./ml.}$	± 0.84	± 0.35	± 0.25	± 0.05
Urine level	196.0	148.0	94.0	58.3
in $\mu\text{g./ml.}$	± 28.0	± 25.0	± 13.0	± 8.2
Total urinary excretion	31.9	27.1	27.0	31.9
in mg.	± 9.2	± 5.5	± 3.7	± 5.2

2. Blood Levels

The composite results of the blood levels are shown in Fig. 1. It will be noted that the blood concentrations during the first eight hours exceed the required antibiotic concentration for bacteriostatic effect. Even 24 hours after a single intravenous injection of 275 mg. of pyrrolidinomethyl tetracycline, potential bacteriostatic levels are still present. After a second and third intravenous dose in the same patients, a cumulative effect was noted in the 12- and 24-hour values.

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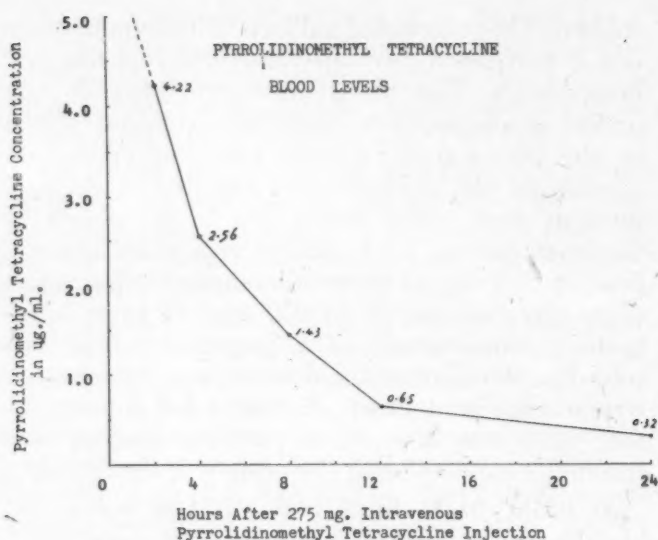


Fig. 1

3. Urine Concentrations

The concentration of pyrrolidinomethyl tetracycline in the urine was significantly high in the 10 cases in which it was assayed, and varied between 124 and 170 $\mu\text{g./ml.}$ for a 24-hour period (Fig. 2). This means that the urine levels 8-24 hours after the injection were 100-200 times higher than the blood levels.

4. Toxicity

Intravenous injection of pyrrolidinomethyl tetracycline produces no local pain. Neither during nor after the injection, which should last one minute, were there any complaints. Some of the patients experienced a taste sensation, similar to ether, during the injection. This disappeared rapidly after the injection was completed. No thrombotic or inflammatory manifestations were encountered, even with frequent injections in the same vein. Allergic manifestations were absent. No enterocolitis occurred.⁵⁻⁸

5. Clinical Results

The high urinary concentrations achieved with pyrrolidinomethyl tetracycline led us to expect good results in the treatment of infections of the urinary tract. Our expectations were fulfilled. The following summaries on four cases illustrate the advantages which pyrrolidinomethyl tetracycline possesses over other antibiotic treatment in specific situations.

CASE 1.—Mrs. F.M., a 62-year-old woman, was admitted to The Doctors Hospital with severe pernicious anemia. Hemoglobin concentration was 4 g. % and erythrocyte count 1,400,000 per c.mm. She was responding to vitamin B₁₂ therapy, when suddenly she developed an acute pyelonephritis with a low-grade fever. Her urine culture grew *E. coli* sensitive to tetracycline. No previous antibiotics had been administered on this admission. Pyrrolidinomethyl tetracycline (Reverin) was given in a dose of 275 mg. intravenously

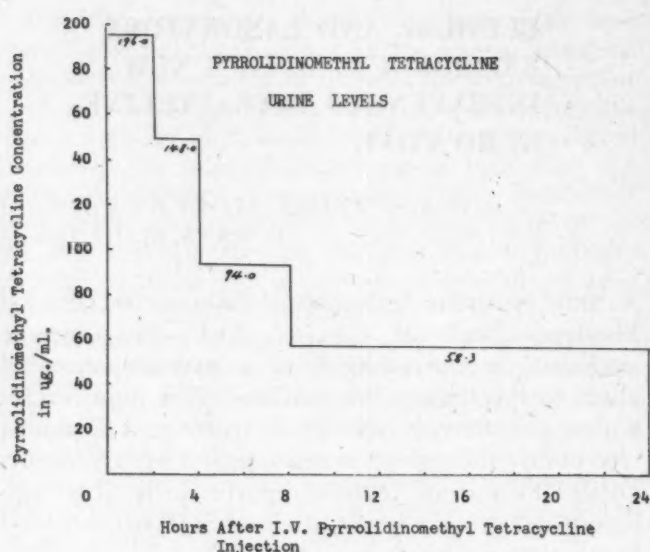


Fig. 2

every day for seven days. The temperature dropped to normal within two days and remained so thereafter. Subsequent cultures remained sterile and a further rise in her reticulocyte count was observed.

CASE 2.—Mrs. E.G., a 38-year-old woman, underwent a subtotal hysterectomy for multiple fibroids. After operation, the patient developed cystitis with many clumped neutrophils in the urine sediment. *E. coli* was cultured, sensitive to tetracycline. Pyrrolidinomethyl tetracycline (Reverin) in a dose of 275 mg. intravenously daily for seven days was given. After this treatment, her dysuria disappeared, the leukocytes in the urine sediment decreased to 2-5 per high-power field, and the cultures remained sterile.

CASE 3.—Mrs. M.V., a 29-year-old woman, was admitted with the diagnosis of an inflammatory pelvic mass. A growth of *E. coli* and a non-hemolytic streptococcus were obtained from a vaginal swab. A penicillin-streptomycin preparation (Dicrysticin) was administered for two days without any improvement. Her fever remained at 103°-104° F. A broad-spectrum antibiotic which could be administered intravenously was indicated. Pyrrolidinomethyl tetracycline (Reverin) was considered the drug of choice since the patient was suffering from nausea and vomiting. After three injections the fever dropped gradually to 99° F. The patient was operated on subsequently and a ruptured appendix, adherent to the right salpinx, was found. Postoperatively she developed cystitis. *E. coli* sensitive to tetracycline was cultured. Another course of six days with pyrrolidinomethyl tetracycline cleared the infection completely. No untoward side effects were encountered during the intravenous tetracycline therapy on either occasion.

CASE 4.—Mr. J.L., a 30-year-old man, was admitted with a perforated duodenal ulcer, 12 hours after the onset of his pain. Operative repair was carried out four hours after admission. There had been widespread peritoneal soiling. Approximately three weeks postoperatively a subphrenic, suprahepatic abscess was drained. Cultures showed a heavy growth of *Staphylococcus aureus hemolyticus*, *Bacillus subtilis* and *Streptococcus viridans*. Drainage from the abscess continued to

grow these bacteria despite chloramphenicol therapy. A change to pyrrolidinomethyl tetracycline (Reverin) in the dosage indicated previously was followed by negative cultures in 72 hours. These cultures remained sterile and the subsequent clinical course was slow but progressive and uneventful thereafter.

DISCUSSION

The undesirable and sometimes very serious side effects of the orally administered broad-spectrum antibiotics are well known.^{2, 3, 5} They relate particularly to the gastrointestinal tract and include vomiting, nausea, and most important, acute pseudomembranous enterocolitis.^{1, 7} In order to reach therapeutic blood levels with these drugs, high dosage is required. Since many factors can influence the efficacy of the enteral route, the levels obtained tend to be variable and often are not dependable. Dosage at least every six hours is required. Should intravenous administration be elected with these antibiotics, continuous infusion is required. This almost always necessitates a hospital setting and implies additional personnel and work. Local vein irritation and at times extensive phlebitis and thrombosis are frequent concomitants of such therapy. Pyrrolidinomethyl tetracycline provides a simple means of attaining a high blood and urinary concentration of tetracycline with a single intravenous injection daily. No undesirable side effects have been demonstrated to date.

SUMMARY

A new synthetic tetracycline derivative, pyrrolidinomethyl tetracycline (Reverin), is extremely soluble in water and can be injected intravenously within one minute without local or systemic complications.

The extensive work in European laboratories with this drug has been confirmed, viz. that therapeutic blood and urine levels are rapidly attained, and in most instances are still present after 24 hours. Ten "normal" patients were used for blood and urine assays and four clinical cases of infection were treated.

In the few instances where it was felt clinically that the dosage interval should be 12 hours, no toxicity was encountered.

It appears that this new drug offers a real contribution to the therapeutic armamentarium despite the host of tetracycline products already available. Its particular attributes make it highly effective where the infection can be countered via the blood stream, and particularly suitable when the site of sepsis is the urinary tract.^{6, 8}

The invaluable laboratory assistance of Mr. Hans Wittfoth and Mr. Colin Wong is gratefully acknowledged. (Detailed assay methods were specifically developed for this project and are available upon request.)

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Mental stress, whether sudden or prolonged, is a potent factor in the aetiology of insanity, although it has doubtless always other factors associated with it, and notably heredity. This is a resultant of our civilization, and depends upon such a variety of conditions that its valuation is most difficult. Nor can it be dissociated from other products of civilization, such as the artificial life of the city, with the crowding in insanitary tenements, the ill-nourishment, the struggle for existence, and the excesses of various kinds so common amongst residents of cities. In all England and Wales, prolonged mental stress is given as a cause in 16.5 per cent. of admissions for a year (1908), while in the London county asylums (1909), it is an assigned cause for nearly 24 per cent. of cases. These figures should perhaps not be compared, as they are gathered from separate reports, and one must always consider the personal element in the compilation of statistics. Yet such element could not account for all of the discrepancy between the figures for London and those for England at large. The influence of city life on the production of insanity is also shown by the figures of the State of New York. In 1908, 76.8 per cent. of the male, and 79.6 per cent. of the female, admissions to the hospitals for the insane of that state were from the cities and large towns, while 90 per cent. of the male paretics and 88.3 per cent. of the female paretics, 81 per cent. of the male cases of alcoholic insanity and 79.6 per cent. of the female cases, came from the large centres of population. We find in these figures a good reason for the cry "back to the land", but the movement towards the cities is growing steadily, and it becomes more and more evident every day that it is here that the work of prevention must be

largely centred. In this we have a problem of increasing magnitude, the solution of which, in the interest of every phase of our social life, must very soon be seriously undertaken.

It is particularly in the cities that alcoholism and syphilis are rampant, and for that reason I venture a few remarks on these conditions. The last (1908) British statistics assign to alcohol the causative role in 22.6 per cent. of the male and 9.9 per cent. of the female admissions to asylums for the year, the average being slightly less than 16 per cent. for both sexes. In the London county asylums, on grouping the sexes, it is found that, of the admissions for 1909, 20 per cent. owed their insanity to alcoholism. Thus again is the influence of city life shown. A full consideration of all the conditions co-related to alcoholism is desirable, and in fact necessary, in order that we may be able effectively to direct efforts to the correction of this evil. The physician must not ignore any factor which is prejudicial to health, and the abuse of alcohol is so well recognized as a common cause of disease that it becomes a duty of every member of our profession to give to it at least as much attention as is given to other causative factors. It may not be easy for us to decide just what attitude we should take towards the prohibition movement, but we should at least never lose thought of the fact that those predisposed by heredity, or otherwise, to psychic or neuric breakdown are singularly susceptible to alcohol and similar drugs, which, in consequence, should be prescribed for them only with the greatest circumspection.—W. H. Hattie, *Canad. M. A. J.*, 1: 1024, 1911.

OBSERVATIONS ON VAGINAL
TRICHOMONIASISII. TREATMENT WITH
METRONIDAZOLE*S. C. ROBINSON, M.D. and
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IN PART I of these communications¹ describing the studies on *Trichomonas vaginalis* infestation that are being conducted at Dalhousie University, the following observations were reported:

1. In pregnant women, the presence or absence of *T. vaginalis* appears to be unrelated to the various other bacteria and fungi which may be present in the vagina; that is, there is no "favourable" or "unfavourable" underlying vaginal flora.

2. Untreated, the parasite remains in the vagina throughout pregnancy and delivery, and can be cultured from the lochia.

3. There appears to be no "favourable" pH range.

4. The presence of *T. vaginalis* in the mother's vagina has no ill effect on her infant.

5. Though "symptomatic" cases are less frequent (8%) than asymptomatic cases, the organism can be obtained by culture from about 50% of the women attending the Dalhousie University Prenatal Clinic.

PROBLEMS IN TREATMENT

Because this organism is harboured by many asymptomatic women—about 40% in our series, which now includes over 1000 pregnant women—and apparently does not harm the child, the question arises "Who should be treated?" At the present time, we know of no means whereby we can predict which patients will develop symptoms. Leukorrhea of itself is such an "indefinite" condition that only the most severe examples can be classified as "symptomatic". The woman who complains of irritation—if she has trichomoniasis—is obviously a candidate for treatment, and those with associated urinary symptoms attributable to this infection may be relieved by treatment.

Heretofore our practice has been to treat those who carry a heavy infection—as determined by the ease with which the motile flagellates are identified on direct microscopic examination of the wet preparation. This policy has resulted in moderately satisfactory results except for those "resistant" or "recurrent" cases which have led to trichomoniasis being called a stubborn disease. In the light of our present limited knowledge, these criteria may be satisfactory.

Previous methods of treatment are innumerable. *In vitro* activity of any particular agent is not necessarily related to its *in vivo* effectiveness. Trus-

sell's² extensive list of preparations tested for *in vitro* activity and *in vivo* effectiveness indicates the magnitude of the search being carried on for the ideal therapeutic agent; and it points clearly to the fact that no ideal agent was available at the time that these studies were reported in 1947. The difficulty of dispersing any trichomonicidal agent thoroughly and continuously throughout the vagina is great. Tablets, jellies, douches, paints, powders, pledgets and ointments all have had their advocates. Furthermore, the parasite may be harboured in the cervix, in Bartholin's glands and in the urinary tract and probably in other sites which are less accessible. However, there is no reason to believe that it survives in the blood stream or lymphatics.³

Our lack of factual knowledge of the epidemiology of this disease makes it almost impossible to institute prophylaxis. It is quite apparent that promiscuous venereal spread cannot explain many of the cases encountered. For the present, we must be satisfied with improved methods for treating known cases.

Criteria for a Satisfactory Drug

A suitable antitrichomonal agent should show the following characteristics:

1. It must be safe—to both the adult and the fetus.
2. It must have greater than 90% effectiveness.
3. It must be administered easily.
4. It must be stable, package easily, and be comparatively economical.
5. It must not be unpleasant to use or have undesirable side effects.
6. The treatment course should not be prolonged, and symptoms must be promptly relieved.
7. It must disperse well and have a potent, rapid local effect.
8. It must be effective in tissue fluids so that it may reach otherwise inaccessible sites.
9. It must be effective in the urinary tract as well.

METRONIDAZOLE

Metronidazole became available to us in 1959 after preliminary clinical studies by Darel *et al.*³ in Paris and Sylvestre, Gallai and Ethier⁴ and Fortier⁵ in Canada. We carried out an independent pharmacological assessment of this substance as follows.

1. Serial dilutions of metronidazole were made and added to actively growing cultures of *T. vaginalis*. Duplicate experiments were carried out and suitable controls maintained; 1 c.c. of 1/10,000 dilution (0.0001 mg. of metronidazole) killed the organism growing in simplified trypticase medium (Kupferberg) in 24 hours, and 1 c.c. of 1/100,000 (0.00001 mg.) was effective in 36 hours. Stronger solutions were more rapid in their action; weaker solutions were ineffective. Therefore, metronidazole is trichomonicidal in concentrations which can be attained in the tissues of the human ingesting

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250 mg. twice daily, if that concentration is maintained for several days.

2. Serum drawn from patients taking 250 mg. of metronidazole twice daily by mouth and control serum were added in decreasing amounts to cultures of *T. vaginalis* of a 10 c.c. volume. The organisms were killed by 0.5 c.c. or more of the serum from treated patients but not by that from controls. It appears that therapeutically effective concentrations of metronidazole are achieved in human serum when the recommended dose schedule is maintained.

3. Urine from treated cases and controls was similarly tested; 1 c.c. added to active cultures killed the parasites in four hours; 0.5 c.c. did not kill all the parasites, and the urine from controls had no effect. It appears that effective concentrations of the drug occur in the urine of patients on therapy with this agent.

Biochemical, pharmacological and experimental biological features of metronidazole have been reported by Cosar and Julou,⁶ who developed the drug.

No serious toxic effects have been reported in adults in the accumulating literature on this substance, but some toxic effects were noted in animal fetuses where large doses were administered to the parent animal.⁷ A small proportion of fetuses died *in utero*, presumably as a result of the huge doses of the drug administered to the pregnant animals; no deaths occurred in the control animals. No problems of this kind have been reported in the human subject.

Most of the criteria which we have established for a suitable trichomonocidal drug were therefore satisfied.

CLINICAL TRIALS

A. Thirty non-pregnant women, all of whom had trichomonads in vaginal culture, were treated, using 250 mg. tablets which were taken orally twice daily for 10 days; no topical therapy was used. Twenty-seven of these patients did not have the organism on subsequent vaginal culture; three patients required one additional course of therapy before the cultures became negative. No intolerance or dyscrasias were noted in the women who were treated, but long-term follow-up was not possible. Because our culture technique is highly accurate¹ and the mechanism of infestation is not known, there does not appear to be any value in long-term follow-up if the individual cannot be isolated. This drug appears to be highly trichomonocidal when given by mouth only. Although this was a small preliminary study, the cure rate, 90% on a 10-day course, is similar to that found in a number of other reported series, most of which are also based on small numbers of patients.

B. One hundred women at the Dalhousie Prenatal Clinic were found to have vaginal trichomoniasis, by smear and/or culture. These were all

treated as follows: They were given 20 250-mg. tablets and instructed to take one tablet by mouth each night and morning for 10 days. They were also given 10 500-mg. tablets and instructed to insert one tablet into the vagina each night for 10 days.

Married women were also provided with sufficient tablets so that their husbands could have a similar course of oral treatment. No other treatment was prescribed. The women were at various stages of gestation when they were treated.

None of the women or their husbands complained of intolerance to or symptoms from the drug, although each was specifically questioned in this regard. Twenty-seven women had symptoms, possibly due to trichomoniasis, such as itching, profuse discharge, or both. In each case, the itching was fully relieved and the discharge disappeared or was greatly diminished.

TABLE I.

Cases treated	Negative smear and culture		
	1 month	2 months	3 months
100	93 (of 100)	41 (of 46) (3 previously negative) (2 previously positive)	11 (of 14) (1 previously negative) (1 positive 1st month) (1 positive 1st and 2nd month)

Gross cure rate (1 month): 93%

The gross cure rate at one month was 93%. Further tests were made on some of the women at two and three months (Table I). Obviously, the possibility of re-infection in some cases cannot be excluded. No attempts at further treatment were made and it was impossible to follow up all the women for an extended period. This was not regarded as an important defect in our investigation, as the gross cure rate, based on an accurate testing method, was highly satisfactory. In 21 cases, the leukocyte count was checked before and one to three weeks after treatment. No significant alteration or abnormality was recorded.

C. The babies of 92 women, including one set of twins, were studied; eight women have not yet been delivered or have left the clinic and their babies are not available for study. These women were delivered in the Grace Maternity Hospital, Halifax, under the supervision of the resident or attending staff. Initial observations of the babies were made by the resident, and a complete physical examination of the infant was carried out at birth and before discharge at one week. During the neonatal period, the infants were examined by the pediatric attending or resident staff. The observations on the babies are recorded in Table II. It is unlikely that any of the few abnormalities noted can be attributed to the absorption of metronidazole by the mother.

TABLE II.—BABIES

Total number.....	93 (1 set twins)
Apgar rating (1 minute):	
Score of 8 or higher.....	89
Score of 7.....	1
Score of 6.....	2
Score of 5.....	1 (breech)
“Congenital” defects	
None.....	90
Umbilical hernia.....	1
Hydrocephalus.....	1
Two small skin tags on right ear.	1
Birth weight	
>6 lb.....	84
<6 lb.....	9 (including 1 twin)
Capillary hemoglobin at birth	
> 17 g.%.....	82
16 - 17 g.%.....	7
15 - 16 g.%.....	3
14 - 15 g.%.....	0
13 - 14 g.%.....	1
Neonatal disease (during the first seven days)	
Severe vomiting.....	1 (recovered)
Pneumonia.....	2 (recovered)
Upper respiratory infection.....	1 (recovered)

DISCUSSION

Since metronidazole was first described in 1959, there have been a number of reports of its use; these are summarized in Table III. All these studies indicate that the drug is more than 90% effective both when taken alone orally, and when taken in combination with topical therapy. In general, our observations agree with those of others regarding the therapeutic effectiveness of this agent. The fact that this substance, when taken orally, reaches concentrations in tissue fluids and urine which are trichomonocidal is of primary importance. We are not aware of any other drug which has shown this property and believe that this quality represents a genuine advance in the treatment of this infection. The drug, by and large, fulfils the other desirable criteria, enumerated above, for a suitable trichomonocidal agent and has replaced the arsenicals as the treatment of choice in this prenatal clinic.

In our experience with the drug, no contraindications to its use have been discovered.

TABLE III.—RESULTS IN WOMEN TREATED WITH METRONIDAZOLE.

Author	Oral therapy		Combined therapy	
	Number	Cure	Number	Cure
Fortier.....	8	4	31	28
	—	—	65	65
Darel.....	—	—	19	17
Watt and Jennison...	50	44	—	—
Moffet.....	28	27	14	13
Robinson and Johnston	30	27	100	93
	116	102 (87.9%)	229	216 (94.3%)

SUMMARY

Thirty women with *T. vaginalis* infestation were treated with metronidazole, a new trichomonocidal substance taken orally; 90% were cured with a single 10-day course; 10% required a second course of therapy.

One hundred prenatal clinic patients who harboured the same flagellate were treated orally and topically; the husbands of these women were treated orally with the same drug; 93% of the women were free of the infection one month later.

No complications from treatment were recognized and the babies born to these women were not adversely affected.

Metronidazole appears to be the treatment of choice for *T. vaginalis* infections at the present time.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Regret is often expressed that common sense is not more generally used in the propagation of the human species, and we are familiar with attempts at legislation aimed at the control of marriage, the sterilization of degenerates, etc. Sentiment, however, is generally against such measures, and doubtless, also, there are better reasons than mere sentiment for opposing them. Something may be done in dealing with the more reasonable sort, by the gentle art of persuasion, the objections to marriage and especially to procreation being set forth tactfully, as one has opportunity in dealing with those in any way predisposed to psychic disturbance. Such instruction might well be undertaken early in life, before any suspicion of a "love" entanglement has to be combatted. When there is evident defect, particularly

if any tendency to eroticism is manifest, the safety of the community, as well as of the unfortunate individual, demands segregation in a suitable institution. This costs more than sterilization or the lethal chamber, but does less violence to sentiment. Some authorities, as Archibald R. Douglas, of the Royal Albert Institution, assert that the imbecile is a much more potent agent in producing racial deterioration than the lunatic. I doubt if we have any more pressing need in Canada to-day than the proper provision for the feeble-minded members of our country, particularly those who are still sexually competent.

At best, we shall, for many years at least, be able to control the production of potential lunatics to only a very small extent.—W. H. Hattie, *Canad. M. A. J.*, 1: 1021, 1911.

SPECIAL ARTICLE

THE HOME-CARE MEDICAL PROGRAM OF THE WINNIPEG GENERAL HOSPITAL*

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INTRODUCTION

THE PATIENT with a long-term illness has medical needs that are not always met by the facilities available in a large general hospital. These needs have been met in several centres by a variety of home-care programs, some community-based, some hospital-based, and some of them catering only to patients with specific diseases or disabilities.¹⁻⁶

Two major considerations led to the establishment of the home-care program of the Winnipeg General Hospital. It was felt that in the majority of cases, patients with chronic illness prefer to be cared for in their homes if help is provided, and that such care is more satisfactory and economical than that provided in hospitals.

While home care is not a substitute for necessary hospital care, it may be expected to bring about a decrease in hospital bed occupancy, particularly since the patient considered most suitable for home care is chronically ill and contributes disproportionately to hospital patient days. The discharge of long-term patients from the Winnipeg General Hospital has been a problem, partly because of the relatively high proportion of indigent patients.

Over the years, various methods have been evolved to facilitate the discharge of long-term cases. The social service department of the hospital was instrumental in determining the patient's social needs and arranging his discharge to his home with the assistance of a number of community agencies. The outpatient department provided care to such patients able to return to that department but lacked facilities to carry care into the home. Patients requiring long-term bed care were discharged to the chronic wards of the Winnipeg Municipal Hospitals and to the nursing homes under the direction of the City Health Department. Home nursing services were provided by the Victorian Order of Nurses whenever requested. However, there were patients who did not fit into any of these categories and others whose transfer to long-term beds tended to block these indefinitely. In many instances, discharge to a nursing home or municipal hospital could be avoided by the provision of equipment, nursing, homemaking services and medical supervision in the patient's own home.

Therefore, in 1957, steps were taken to establish a home-care program in the Winnipeg General Hospital to be administered from the outpatient department with funds from Federal-Provincial health grants. The program came into effective operation in August of 1958. Numerous enquiries and visits from interested persons in other centres have prompted us to publish our experience to date.

REQUIRED FACILITIES

Since the hospital already had at its disposal a wide variety of services which have been previously mentioned, the major requirement in setting up a home-care program was the establishment of a central office in the outpatient department, the acquisition of a few additional personnel, funds, and the administrative authority to co-ordinate all these facilities as described in the following sections. In establishing a home-care program it was planned that duplication of services already available in the community would be avoided.

METHOD OF OPERATION

Referrals are received from the wards of the Winnipeg General Hospital and Municipal Hospitals, from the outpatient department of the Winnipeg General Hospital, from private physicians and from other agencies outside the hospital, such as the Victorian Order of Nurses. The patients are referred by attending doctors, interns, nurses and social workers. Each case is assessed by the nursing co-ordinator and the medical co-ordinator, to determine suitability and requirements for home care, since all cases are not suitable for such services. Those patients whose care is particularly complicated are usually referred to nursing homes or to the chronic wards of the Winnipeg Municipal Hospitals. Patients with advanced heart disease or malignancies, who are unable to return to the outpatient department or to the doctor's office, can very often be managed easily at home with the provision of nursing aid and medical visits. Some patients and their relatives are elderly, and without the provision of homemaking assistance they cannot assume the increased work load imposed by a bed-ridden patient. A small group of cases suitable for home-care services are patients with advanced respiratory disease requiring the frequent administration of oxygen under pressure. The bedridden case of multiple sclerosis has also proved to be suitable for home care, as have patients with a wide variety of other conditions.

The patient is discharged to his home once satisfactory arrangements have been made for his

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continued care in that setting. Nursing and homemaker visits are arranged as advisable, and periodic reports regarding the progress of the patient are obtained from the nursing and home-making personnel. Day-to-day problems in management are handled by the nursing co-ordinator and the medical co-ordinator of the plan. Where required, medical visits are made by the resident house staff or the patient's physician. No attempt is made to supplant the functions of the outpatient department or to provide full hospital services in the home. The patients return to the outpatient department of the hospital or to their private physicians for treatment and investigation that cannot easily be given at home. In certain cases, re-admission to hospital is arranged to facilitate intensive treatment of the patient or to provide relatives with a welcome vacation from the responsibility of caring for home-care patients. All patients in the program are reviewed weekly by the medical and nursing co-ordinators in an effort to maintain a high standard of medical care in the home.

PERSONNEL

The medical co-ordinator (part-time) supervises the program and makes the original decision as to selection of cases. He is assisted in the day-to-day medical supervision of home-care patients by a part-time medical assistant.

The nursing co-ordinator was obtained through the auspices of the Victorian Order of Nurses and she has proved to be an essential part of the home-care program. As has been mentioned, for many years the Victorian Order of Nurses has provided home nursing to patients in the Winnipeg area, and because of their considerable experience in this field, it was felt that the necessary co-ordination of medical and nursing needs could best be met by a nursing co-ordinator from the ranks of that organization. A great deal of the nursing co-ordinator's time is spent in organizing the home-care needs of patients and handling the patients' day-to-day requirements.

The secretary serves an important role in the program, handling the records as well as answering the large number of telephone calls from both patients and interested agencies, which are directed to the home-care office. The easy accessibility of the secretary and the nursing co-ordinator by telephone has proved to be a major reason for the success of the program. It has been found that patients and relatives derive considerable comfort and reassurance and require fewer doctors' and nurses' visits as a result of easy and frequent telephone communication with the home-care office. The secretary and the nursing co-ordinator also arrange the provision of medications, equipment and nursing supplies for the patients.

The provision of homemaking services is a major problem. This service is supplied by the Family Bureau of Greater Winnipeg, which has given

every assistance. However, it is apparent that the supply of homemakers is limited and occasionally patients must remain in the hospital longer than necessary before a suitable homemaker can be found.

Without the resources of the social service department and the outpatient department of the hospital, the home-care program could not function adequately.

The social service department comprises six trained medical social workers, all of whom contribute valuable services to the home-care plan. The hospital social workers very often are aware of problems arising from the discharge of patients and will frequently initiate a patient's referral for home-care services. In addition, the social worker's special knowledge regarding the provision of welfare benefits is utilized in many ways to implement home-care arrangements. Without this sort of assistance, a full-time medical social worker would be required. The nursing co-ordinator, as a result of long experience with the Victorian Order of Nurses, is cognizant of many of the social needs of the patients, and because of her previous experience knows where assistance can be found. As the volume of patients increases, it is possible that the employment of a full-time medical social worker may be necessary.

The outpatient department is of great value in facilitating home care. Many patients are brought back to the outpatient department for diagnostic tests and treatment that cannot be given at home. Without the availability of these facilities, the economic and satisfactory operation of the program would be much more difficult, although we are aware of home-care programs in other centres which are community-based and not hospital-based.

ANALYSIS OF THE HOME-CARE CASES

Since the inception of the home-care program in August 1958, 178 patients have received home-care services. The great majority of the cases were accepted during the past year, as indicated in Table I.

TABLE I.

	No. of cases	Days of care
Aug. 1/58 - Sept. 30/60 (26 months)	178	33,598
Oct. 1/59 - Sept. 30/60 (12 months)	151	24,617

The major diagnoses of these patients are outlined in Table II.

The remainder of the statistics deal only with the last 12-month period (October 1, 1959, to September 30, 1960). During this time, 151 patients received home-care services. Sixty-five of these were discharged from hospital under the program and 86 were enrolled from outside the hospital. The majority of these patients, 130 in number,

TABLE II.

Major diagnoses in all cases		
Chronic heart disease.....		36
Arteriosclerotic and hypertensive.	24	
Rheumatic.....	12	
Chronic pulmonary disease.....		22
Emphysema.....	17	
Others.....	5	
Advanced malignancy.....	35	
Neurological disease.....		
Cerebrovascular.....	25	
Neurological (e.g. multiple sclerosis).....	20	
Paraplegia.....	5	
Fractures.....	4	
Rheumatoid arthritis.....	7	
Others.....	24	
Total.....	178	

were indigent; the remaining 21 were private patients. The sex distribution was 90 females and 61 males. The age distribution is shown in Table III.

It may be seen from the age distribution (Table III), and from Table II, that most of the patients were elderly and were suffering from chronic degenerative and neoplastic diseases. It is not surprising that 38 died while on home care during the year, and that 59 of 151 patients required 76 re-admissions to hospital. However, 29 were discharged from the program, as they no longer required this type of care. At the present time, the daily census of patients fluctuates at about 100, which seems to be optimal for the present staff and facilities.

TABLE III.

Age (years)	No. of cases
0 - 10.....	2
10 - 20.....	4
20 - 30.....	2
30 - 40.....	7
40 - 50.....	9
50 - 60.....	22
60 - 70.....	28
Over 70.....	77

The following case report illustrates many of the problems encountered in providing home care:

Mrs. P., aged 75 years, had suffered a traumatic paraplegia some years before and required several periods of hospitalization because of bladder infections, decubitus ulcers and increasing senility. In June of 1958 she was on a chronic-care ward in the Winnipeg Municipal Hospital and it seemed likely that she would remain there. However, her husband, who was 75 years of age, was very anxious to have her at home, and she was accepted for home care in June 1958. The family was indigent and the home contained the bare necessities. A hospital bed, wheelchair, bedpan, and other minor nursing aids were provided. The Victorian Order of Nurses visited the patient at daily or twice-daily intervals to provide nursing care, and the Family Bureau provided housekeeper services from time to time to help with heavy cleaning. Dressings and pads required for the patient's care were obtained from the Winnipeg General Hospital and medications were obtained in the usual way through the hospital outpatient

department. On several occasions the patient was brought to the outpatient department for treatment and on two occasions she was admitted to hospital for 16 days and 12 days, for intensive treatment of her bowel and bladder disorders.

ECONOMICS

The cost of the various services provided during the year is set out in Table IV.

The average per diem cost per patient was \$1.78, of which administration costs account for 52 cents. This does not include drugs which are supplied from the Winnipeg General Hospital Dispensary under the same arrangements as are applicable to all outpatients.

TABLE IV.—USAGE OF HOME CARE SERVICES IN THE PAST YEAR (151 CASES)

	Cost
Home nursing —136 cases.....	\$14,192.
Housekeeping — 50 ".....	9,863.
Equipment — 19 ".....	955.
Transport — 88 ".....	1,197.
Physiotherapy — 5 ".....	315.
Supplies — 36 ".....	1,802.
Doctors' house calls— 98 ".....	2,370.

In order to assess roughly the financial saving, which is of course not the prime reason for the program, all cases were reviewed. From our experience with these and similar cases, the saving of hospital and nursing home bed days was estimated and is depicted in Table V. Under the heading of "hospital days" we have grouped together the acute hospital bed and chronic or long-stay hospital bed days that we consider had been saved.

TABLE V.—SAVING OF BED OCCUPANCY

	Days	
	Hospital	Nursing home
Aug./58 - Sept. 30/60— 178 cases (26 months).....	15,930	12,733
Oct. 1/59 - Sept. 30/60— 151 cases (12 months).....	12,069	9,919

COST SAVING

Cost of:	Hospital care	Nursing home care	Home care	Saving
Aug./58 - Sept. 30/60 (26 mos.).....	\$286,470	\$47,749	\$66,059	\$268,430
Oct. 1/59 - Sept. 30/60 (12 mos.).....	217,242	37,196	43,736	210,702

This past year's saving of hospital and nursing home days is approximately equivalent to full occupancy of 33 hospital and 27 nursing home beds. In addition, since the beginning of the program, re-admissions to hospital have been prevented or earlier discharge achieved in 32 cases, 18 of whom were cared for in this program during the past 12-month period.

In Winnipeg, an average hospital bed costs \$18.00 per day and a nursing home bed \$3.75 per day. The cost saving can, therefore, be roughly estimated.

DISCUSSION

The home-care program has now been in operation for 26 months and certain conclusions can be drawn from our experience. There are real benefits to be gained from the institution of a home-care plan. With such services available, patients can very often be discharged earlier than would otherwise be the case, and in many instances, with adequate home care, re-admissions to hospital can be prevented. In both of these ways, active hospital beds can be saved and utilized in a more advantageous manner. There is also a financial saving which is readily apparent from the data presented.

More important is the benefit of the home-care program to the patient, which has been its most gratifying aspect. It has been the experience of everyone associated with this program that patients and their relatives are happier and much prefer medical care in their homes to institutional care, if they are adequately supported. Initial reluctance on the part of relatives to assume responsibility for the long-term care of chronically ill patients has invariably been rapidly dispelled by the knowledge that the resources of the home-care program are available to them on a 24-hour basis.

A further benefit has resulted from the involvement of medical students and interns in the home-care program. For some time, fourth-year clinical clerks have been assigned in rotation to various families receiving home care and have participated in their management under the supervision of the intern staff and the medical co-ordinators. In this way, students and interns have been made aware of the long-term problems of chronic care and have

observed the advantages of a home-care program. It is expected that this will result in an increased awareness of the possibilities of home care.

The most important requirement for the successful operation of a home-care plan is the provision of adequate medical and nursing attention. In addition, however, there must be a small central staff who can co-ordinate the various services required for the successful management of the patient at home. In our experience, this can only be achieved in a situation where doctors and nurses are continuously available, as they are in the outpatient department of any large hospital. It also seems important to us that interested and co-operative personnel must be chosen to ensure the successful establishment of a home-care program.

There are some limiting factors. One of these is the homemaking services, as the availability of competent homemakers is not always adequate to deal with the demands. Patient referral does not necessarily occur spontaneously, and active case-finding on the part of the home-care team is necessary if adequate utilization of hospital beds is to be achieved. It seems to us that case-finding will always be an important function of the home-care team, particularly in the earliest stages of such a program.

In conclusion, we feel that the home-care program described in this report has proved to be of real benefit in a variety of ways. It was initiated as a pilot project, but in only two years of operation it has become a firmly established service of the hospital outpatient department.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE PROPRIETARY SCHOOL

The last vestige of the proprietary school of medicine has passed away from Canada, and medical education is now wholly in the hands of the universities. The change has been forced by the inexorable march of science these forty years past. In the outset all schools of medicine were in reality, if not in obvious appearance, proprietary schools. One was an adjunct to a hospital; another arose out of rivalry; and more had their origin in personal ambition or in professional strife.

It was easy in those days to open a medical school. All that was required was a few bodies for a perfunctory dissection, and a lecture room in which the professor could recite an elaborate epitome of his text-book, or relate the experiences which he encountered upon his daily rounds. If a microscope or two were added, then the equipment was

complete. Access to a hospital was a manoeuvre to bewilder a rival rather than an integral part of the course. It was easy, also, to obtain a faculty at a time when the armamentarium of a surgeon was a knife and a piece of string, and his mental equipment a resolution to let blood; when the main qualification of a professor was a sure facility in speech and a certain capacity to entertain.

Students, too, were not hard to come by. The man who was tired of being a tailor, who found irksome the laborious monotony of the farm, or the man who would improve his social and financial status in the world,—all these were eager to avail themselves of the services of an institution which was willing to minister to their ambition on such easy terms. Even the length of the session was made as short as possible, so that needy students might return to their legitimate and gainful employments with the least delay.—Editorial, *Canad. M. A. J.*, 1: 1091, 1911.

CASE REPORT

VARIANT ANGINA PECTORIS OF PRINZMETAL

DWIGHT I. PERETZ, M.D.,*
West Vancouver, B.C.

IN 1772, HEBERDEN^{1,2} described a non-exertional form of angina pectoris before the Royal College of Physicians in London. Since that time others have been fascinated by this type of angina, and several have published reports concerning it. In 1957 Prinzmetal first reported on 32 cases of this disorder before the American College of Chest Physicians. In 1959 he and his colleagues³ published a preliminary report and established definite criteria for this syndrome, termed "variant angina". The case described in this report fulfils these criteria.

It is important that this syndrome be recognized by the physician because of the poor prognosis that it connotes. It is possible that the prognosis could be improved with early and correct therapy. This syndrome is in most respects diametrically opposite in symptomatology and electrocardiographic findings to classical angina pectoris. For this reason these patients may be labelled "psychoneurotic" by physicians who are not aware of the syndrome.

In 1958, a 50-year-old white male office worker of Scottish ancestry complained that he had been suffering from sudden onset of "pressure in the chest which surges up into my neck and jaw" for the preceding four years. These complaints were not associated with exertion and usually occurred in mid-afternoon. The patient often experienced several attacks at intervals of a few minutes if he did not use nitroglycerin to arrest them. He would occasionally use several tablets of nitroglycerin daily to abort the sense of pressure and constriction. The effect of a single sublingual tablet of nitroglycerin was prompt but usually did not last for any length of time. He did not have chest pain while walking home from work, 13 blocks uphill.

The patient weighed 164 lb. and was 5 ft. 9 in. in height. His heart sounds were distant and no murmurs were heard. His systolic blood pressure varied between 145 and 155 mm. Hg, and his diastolic pressure between 90 and 100 mm. Hg. His pulse rate was consistently within normal limits. His hemoglobin was 15.6 g. % and the Venereal Disease Research Laboratory test for syphilis was negative. The glucose tolerance test was normal. The patient had a normal exercise tolerance for a man of his age. Several electrocardiograms had been taken in the office, and a Master's two-step test had been performed. These tracings showed T-wave inversions in the left ventricular leads but no ST segment deviation. The exercise tolerance test was negative.

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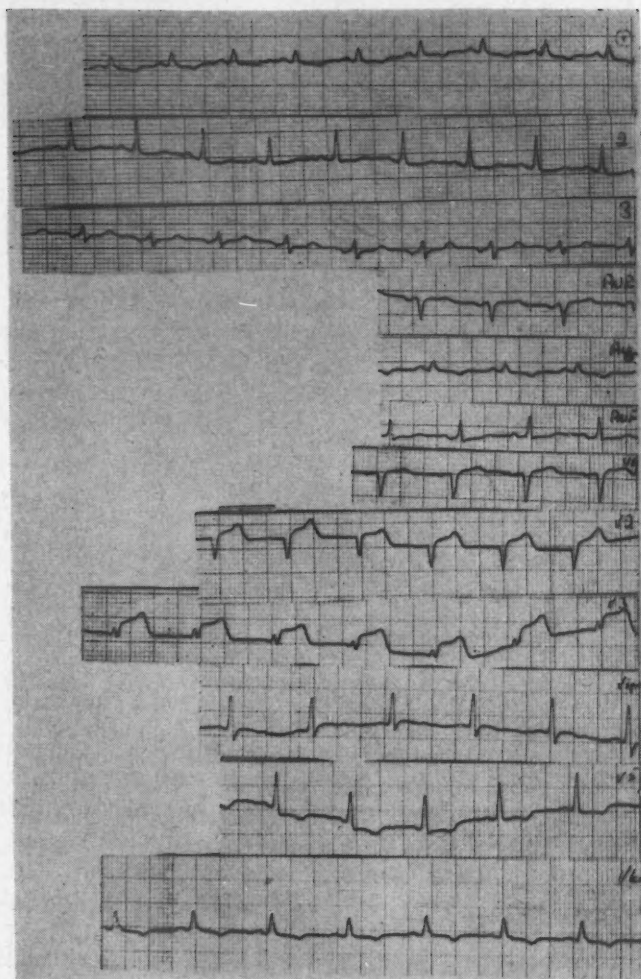


Fig. 1.—Electrocardiogram during an attack of Prinzmetal's variant angina in a 50-year-old male.

One afternoon in March 1958, while a resting cardiogram was being taken in the office, this man stated that he was starting to have his typical chest pain. Fig. 1 shows this electrocardiogram. The occurrence of this patient's discomfort correlated remarkably well with the elevation in ST segment seen on the electrocardiogram. The pain commenced as lead V1 was being taken and ceased as the recording of V3 was being completed; the episode lasted about one and a half minutes. No nitroglycerin was used to treat the discomfort during the attack.

Fig. 2 shows another tracing taken five minutes after Fig. 1. This electrocardiogram was interpreted as showing evidence of acute coronary insufficiency; the patient was advised to moderate his activities and was placed on long-acting nitrites. This medication did not relieve his attacks of chest pain. The patient used alcohol in rather large amounts; he claimed this practice consistently decreased the number of attacks.

Nine months after these electrocardiograms were taken, the patient exerted himself at a square dance in the early evening. One hour after coming home he experienced chest pain and within a few minutes he was dead.

At autopsy the pathologist reported that the heart weighed 480 g. There was hypertrophy of the left

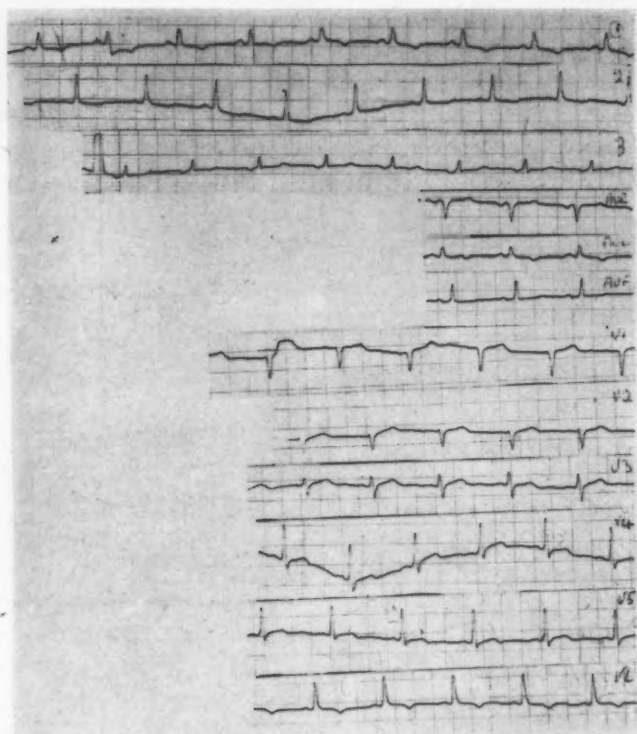


Fig. 2.—Electrocardiogram taken five minutes after attack.

ventricle, with pallor in the anterior wall, chiefly in the septum and the inner half of the muscle wall. There were no valvular defects. The left coronary artery showed marked stenosis over a short distance, 1.5 cm. from its origin. There was evidence of generalized atherosclerosis of the coronary arteries.

DISCUSSION

The features of this case fulfil the criteria defined by Prinzmetal for the diagnosis of variant angina pectoris.^{3,5} The pain occurred while the patient was at rest or during ordinary activity and was not brought on by exercise. The location of the pain was identical with that of classical angina pectoris. The pain was occasionally cyclic in nature and would often recur at approximately the same time each day. The administration of nitroglycerin would promptly relieve the attack. An electrocardiogram taken during an attack showed striking ST segment elevation with reciprocal depression. The area of the myocardium which gave rise to the ST segment elevation during the attack was shown at autopsy to be the area involved in his final myocardial infarction. Contrary to the findings in most of Prinzmetal's cases, the R waves did not become taller or broader. Finally, exercise did not provoke electrocardiographic changes.

It has been suggested that the variant type of angina pectoris results from a temporary spasm of one of the major coronary arteries which is already partially occluded.³⁻⁵ Thus a normal increase in artery wall tone would obliterate the short stenosed area. Prinzmetal *et al.* have provided excellent evidence in favour of this explanation of the pathophysiology of variant angina. These workers also have experimentally reproduced the

electrocardiographic changes seen in this syndrome in 25 dogs, by intermittent occlusion of a large coronary artery. They have advanced the suggestion, supported by experimental evidence, that the ST segment reversal from classical angina pectoris is due to reversal in gradient of intracellular and extracellular sodium and potassium in the two forms of angina.⁵

Prinzmetal has also presented clinical evidence of the effectiveness of nylidrin hydrochloride (Arlidin) in preventing attacks of variant angina.

SUMMARY

The case of a 50-year-old man who fulfilled Prinzmetal's criteria for the diagnosis of variant angina pectoris is presented with electrocardiographic and autopsy findings. Such cases are important to recognize because of their unusual history and poor prognosis if untreated. A review of the literature is outlined.

I would like to thank Drs. T. R. Harmon, pathologist, J. A. Osborne, cardiologist, and O. K. Litherland for their aid and criticism.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE STATISTICS OF INFANTILE PARALYSIS

As little was known regarding the mortality statistics of infantile paralysis, and still less respecting the morbidity of the disease, the Commission of Conservation sent out in November last a circular letter of enquiry with blank return forms to the physicians of Canada. Of the eight thousand letters sent out, replies were received from three hundred and sixteen medical practitioners, and in this manner the histories of six hundred and fifty-eight cases were reported as occurring between November 1st, 1909, and October 31st, 1910. These cases are divided by provinces in the following manner:

DOMINION OF CANADA

Ontario	354
Quebec	187
British Columbia	48
Alberta	27
Manitoba	17
New Brunswick	12
Saskatchewan	6
Nova Scotia	6
Prince Edward Island	1
	<hr/> 658

As to sex incidence, of five hundred and twenty-eight cases, when stated, two hundred and ninety-three were males and two hundred and thirty-five females.—C. A. Hodgetts, *Canad. M. A. J.*, 1: 1036, 1911.

SHORT COMMUNICATIONS

THE PROBLEM OF CENTRALIZATION OF CYTODIAGNOSTIC LABORATORIES

ALEXANDER MEISELS, M.D.,* *Quebec, Que.*

IN CANADA there has recently been considerable discussion concerning the advisability of centralizing certain laboratory facilities, especially those of the cytodiagnostic laboratory. This discussion has been prompted by two divergent viewpoints.

On one side are those who urge the need for cytodiagnostic facilities at the individual hospital level, because they say that only this arrangement will allow close co-operation between the cytopathologist, the tissue pathologist and the clinician. This collaboration is essential for a correct interpretation of the cytological findings and for an adequate follow-up of the cases. This arrangement will permit not only an assessment of the value of the cytodiagnostic method, but also the establishment of certain research projects related to clinical cytology.

On the other side are those who argue that centralization is necessary in order to accumulate sufficiently large series for statistical evaluation. They insist that this is the only solution to the problem that will effectively put cytology at the disposal of every practising physician without the limiting factor of case selection that operates in the local hospitals. Since cytology is now being widely employed as a detection method, and since the objective is to screen as many individuals as possible from a given population, only the facilities of a centralized, well-organized laboratory would prove adequate to handle the very large number of smears expected from such a program.

The existence of such divergent views can best be explained on the basis that both contain a great deal of truth. The advantages of decentralization and centralization, as stated above, are clear enough. But so are the disadvantages of each of the systems:

Against centralization, there is the obvious danger of building up a huge factory-like laboratory, manned mainly by cytotechnologists, in which cytodiagnosis becomes a mechanized, unclinical and unscientific routine. In this atmosphere a large and very interesting series of cases may be lost to final analysis through lack of proper clinical and histopathological correlation.

On the other hand, separate cytology laboratories in local hospitals are self-limiting in scope because of the extreme selection of cases, and their exist-

ence represents a very wasteful duplication of personnel and facilities. There simply are not enough trained cytopathologists and cytotechnologists available to organize and operate so many individual laboratories. Also, the cytodiagnostic service would not be readily accessible to private physicians for the routine screening of their patients.

Another factor that further complicates this situation is the urgent need for training centres where new cytopathologists and cytotechnologists can be produced. These centres should be able to offer more than the usual "on the bench" training facilities.

Confronted with these different considerations, a very promising solution was found, which is now in operation in the area of Quebec City. Under the direction of Professor Carlton Auger, a laboratory of cytology was organized in the Department of Pathology at Laval University. The funds for this were made available through a Federal-Provincial Grant. This laboratory is centralized in the sense that it began offering cytodiagnostic services to all hospitals and private physicians in the area. Two hospitals in the city of Quebec already had cytology laboratories and were not included in the plan. All the pathologists in the Department co-operated in this project from the beginning and made its establishment possible. They provide the means for the clinical and histopathological correlations and make available to the staff members of the cytology laboratory any clinical information that is requested. As the volume of diagnostic work increases, it is planned to establish sections of the cytodiagnostic laboratory in the more important hospitals in order to decentralize the routine workload. These sections are to be staffed by specialized personnel trained at the central laboratory. Eventually, the cytology laboratory at Laval will operate with the following general objectives: to offer cytodiagnostic services to all practising physicians in the area, for the benefit of their private patients; to perform this same service for those hospitals whose annual volume of smears does not justify the establishment of such a service on the hospital premises; to co-ordinate and supervise the activities of the individual cytology laboratories (sections) to be established in the larger hospitals of the area served; to organize, co-ordinate and supervise population-wide screening projects; to train cytotechnologists in a postgraduate course in the Laval Medical Technology School; to train cytopathologists by means of a postgraduate course for physicians; to provide special courses on cytology for medical students and students in medical technology, in connection with the teaching of pathology; to provide for lectures to medical groups on the subject of cytological methods; to undertake

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basic research projects in the field of exfoliative cytology.

This plan is now well under way and action has been initiated, directed to the foregoing nine objectives.

This project represents an eclectic solution to the centralization problem of cytology laboratories. This is certainly a centralized laboratory, but one that is established under the guidance and control of a university pathology department, and with an intention of decentralizing by means of sections in the various hospitals. It has the advantages of processing enough smears to become a useful teaching and research centre, of maintaining through the co-operation of the pathologists, adequate clinical and histopathological control of individual cases, and of co-ordinating the cyto-diagnostic work performed in the whole area.

The importance of a cytology laboratory oriented toward teaching and research can hardly be overemphasized today, when the lack of trained cytopathologists and cytotechnologists is so acutely felt all over the country. Although this is possible only in a partially centralized laboratory, the proper conditions necessary for such centralization should be emphasized: the laboratory should preferably be established within a university department of pathology; it should concentrate on organizing, as early as possible, sections in the leading hospitals, a step towards decentralization; and it should be assured of proper clinical and histopathological control of the cases studied.

Only under such conditions can a centralized cytology laboratory fulfil its purpose usefully and, by providing for earlier detection, play its proper role in the fight against cancer.

PHOTOGRAPHIC ILLUSTRATION FOR MEDICAL WRITING*

V. PROOFS OF ILLUSTRATIONS FOR PUBLICATION

DONALD J. CURRIE, M.D. and
ARTHUR SMIALOWSKI, *Toronto*

THE ENGRAVER receives from the editor of the publishing firm the photograph and the editor's directions as to the method of reproduction and the dimensions of the illustration as it will appear in the publication. An engraving is made to the publisher's specifications. Several test impressions or proofs of the illustrations are printed, and the engraver will forward these to the publisher for approval. The editor of the publishing firm will review the proofs, noting corrections and queries for the author. He will identify each illustration by the figure number and the author's name. The author will receive from the publisher the engraver's proofs of the illustrations as well as the printer's proof of the text and legends. It is the author's duty to approve all of the proofs and to indicate any changes or corrections.

ENGRAVER'S PROOF

Engraver's proofs of illustrations are usually impressions on coated paper. Some smudging or faults in ink distribution can be overlooked in these proofs, as they are only preliminary impressions of the illustrations. Faults other than those due to

smudges and ink distribution should be brought to the publisher's attention for possible correction.

Proofs showing both illustrations and text are made to show the author the relationship of the illustration to the text and legend. These are usually printed on very rough paper and they should not be taken to indicate the final quality of the illustrations. In the case of a medical article, it may be a galley proof; or for a book, a page proof.

One set of engraver's proofs and one set of galley or page proofs is returned to the publisher, answering his queries and indicating the author's approval or noting corrections to be made. The author is expected to make corrections but should not have to make any alterations. Proofs should be studied and returned promptly in order to avoid delay in publication. Where a mistake is found in the original illustration (e.g. a misspelled word), a new original will have to be made and the engraver will be asked to make a new engraving (Fig. 1).

The engraver's proof of each illustration is approved by the author, who must also check the figure number with the legend. Arabic figures, rather than Roman numerals, are used for figure numbers. When writing a book, it is frequently unnecessary to refer to illustrations by number in the text because of the legends and the proximity of the illustration to the related text; this will greatly simplify the revision of text and the re-numbering of illustrations. In the case of journal articles, however, reference to illustrations by number in the text is desirable.

GALLEY PROOF OF TEXT

A galley is a shallow tray which holds a number of lines of type for the text, and a galley proof is a rough printing of this portion of the text. The

*From the Departments of Surgery and Photography, St. Michael's Hospital, Toronto. This is the final communication in a series of five which have been published in successive issues, beginning with the issue of October 14.



a

normal or soft grade is used for exhibitions as glass prints may have objectionable reflections when examined for display purposes. diffusing glass is necessary for even light distribution. Viewing boxes containing a series of low intensity tungsten bulbs regularly spaced

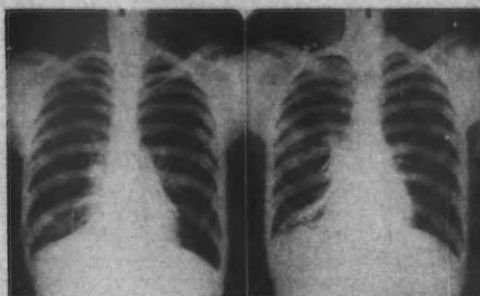


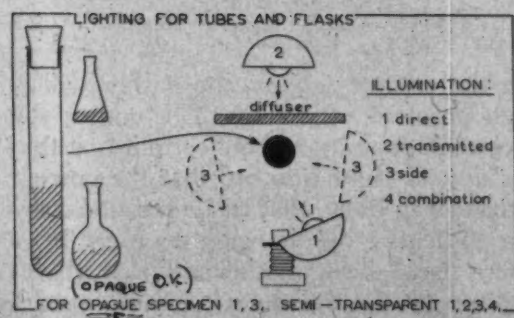
Figure 11. Two Bronchograms of the Same Patient Showing Right Lower Lobe Bronchiectasis. Comparative copies of radiographs are used to show two different views for comparison. This may be made by photographing the radiographs side by side, printing them side by side from separate negatives or composite mounting.



b



Figure 10. Head Supports for Immobilization. An examining chair with a support for the back of the head is shown on the left and a forehead and chin support is shown on the right.



c

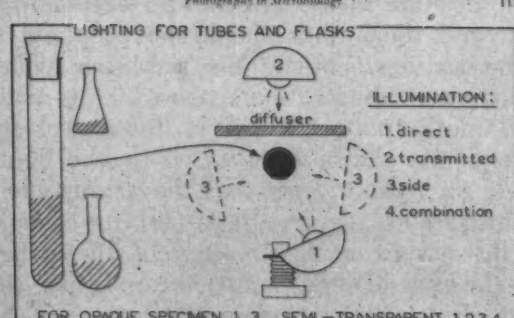


Fig. 1.—Common mistakes found in the engraver's proof which require correction. (a) Publisher's query of the numbering of a grouped illustration and the author's explanation. (b) To maintain uniformity, the author requested a white dividing line between the two photographs. (c) A mistake in spelling found by the publisher which required a correction of the original and a new engraving.

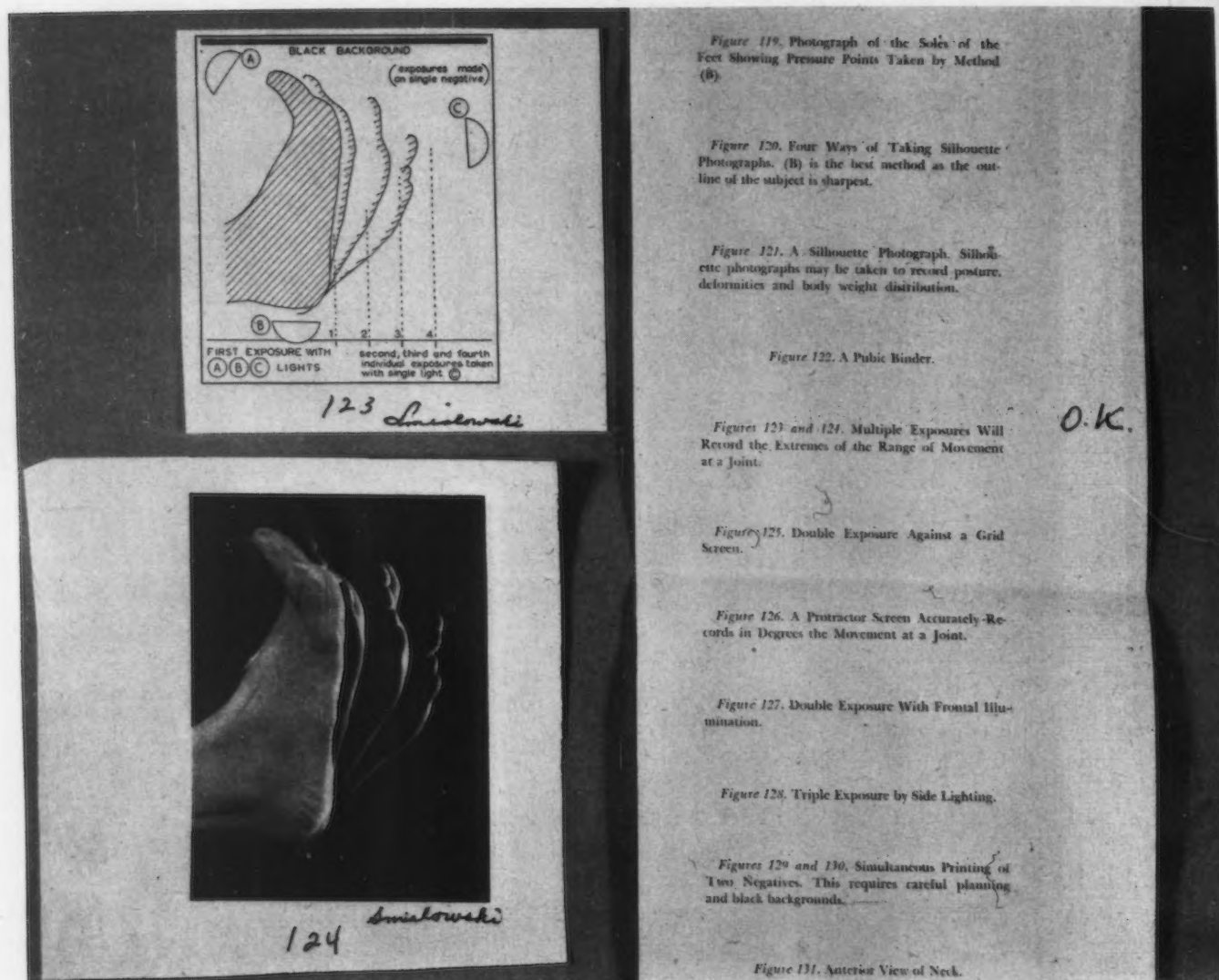


Fig. 2.—The numbering of the legends must correspond with the galley proof of the legends. Most publishers will ask their authors to initial each item on approval.

galley proof is a long column of text set into type as it might appear in publication and it is sent to the author for corrections (see Fig. 2).

After the corrections are made in the galley proofs the author may indicate where in the writing he wishes the illustration to appear. In a short article the position of the illustrations need not be indicated, and the author should be prepared to accept the arrangement by the publisher which will be done according to the space which is available. The only important factor in this case is the correct sequence which is indicated by the figure number. If the author feels that the arrangement of his illustrations is very important, he should indicate his wishes in the margin of the galley proof. In the case of lengthy articles or books, the placement of the illustration in the text must be indicated in the margin of the galley proof by the figure number and an arrow. This marking is for the direction of the compositor who will follow these directions as closely as possible in arranging the text, illustrations and legends for each page. Where the author wishes to have several illustrations arranged in special relationship to each other, for example, on facing pages, these directions

should be given in the margin of the galley proof, in instructions which are submitted with the original illustration and on the engraver's proof of each illustration (Fig. 3). Special arrangements such as "ganging" or "tipping" in illustrations are made on consultation between the author and publisher.

PAGE PROOF

In the case of a book, the author will receive a rough proof of each page. The author should approve each page by making certain that the illustrations appear right side up, that the correct legend is adjacent to them, that the corrections which have been indicated on the galley proofs of text and legends have been made, and that there are no mistakes in the headings or numbering of the pages. The page proofs are submitted only for the author's review and approval; major alterations should not be made at this stage.

Proofs of illustrations are checked by the author for identification, quality and orientation. The importance of checking proofs of illustrations increases with the number of illustrations in the writing.

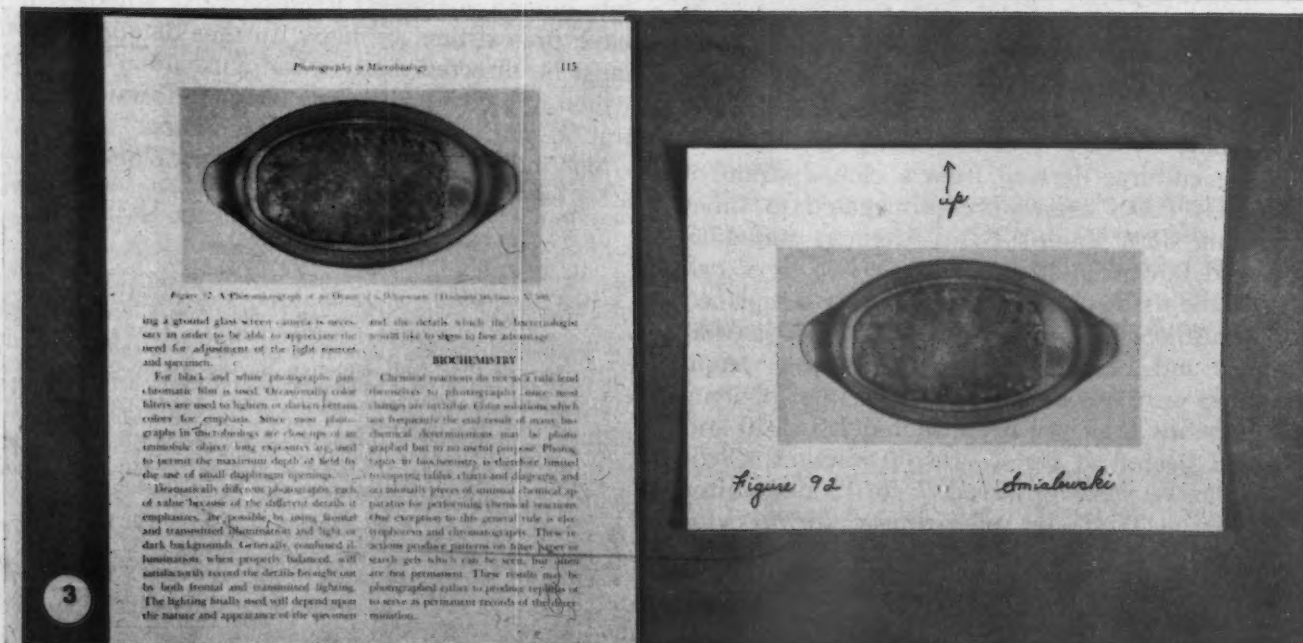
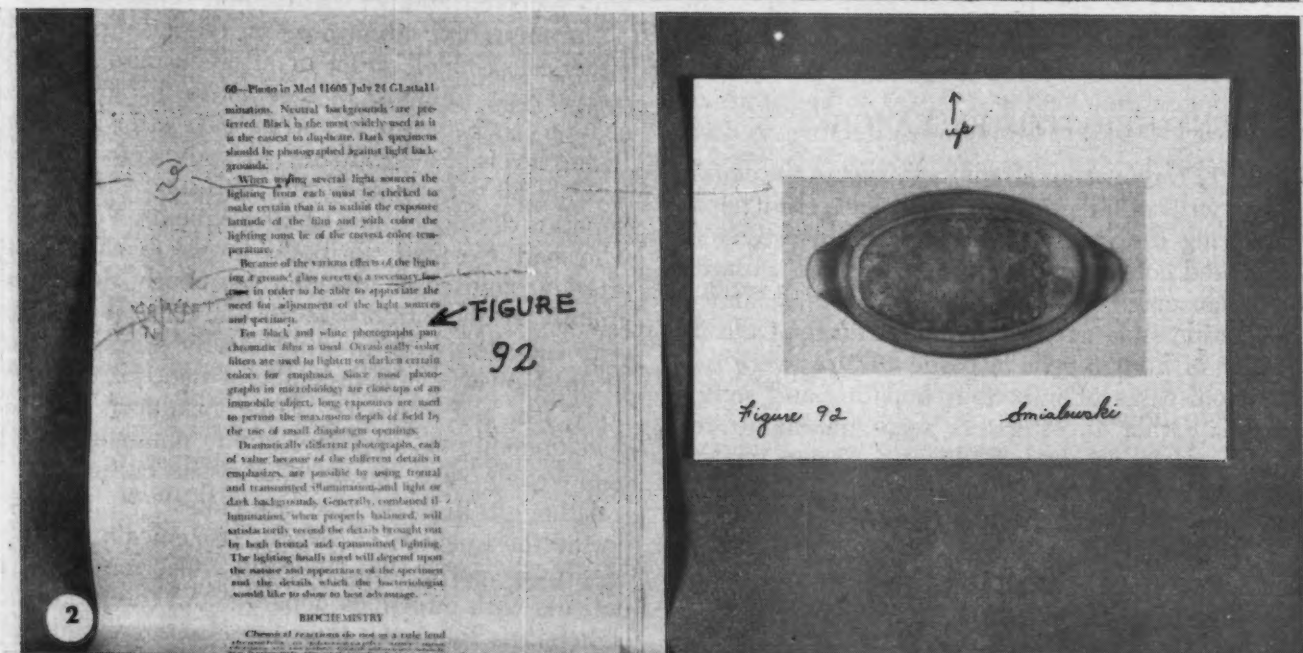
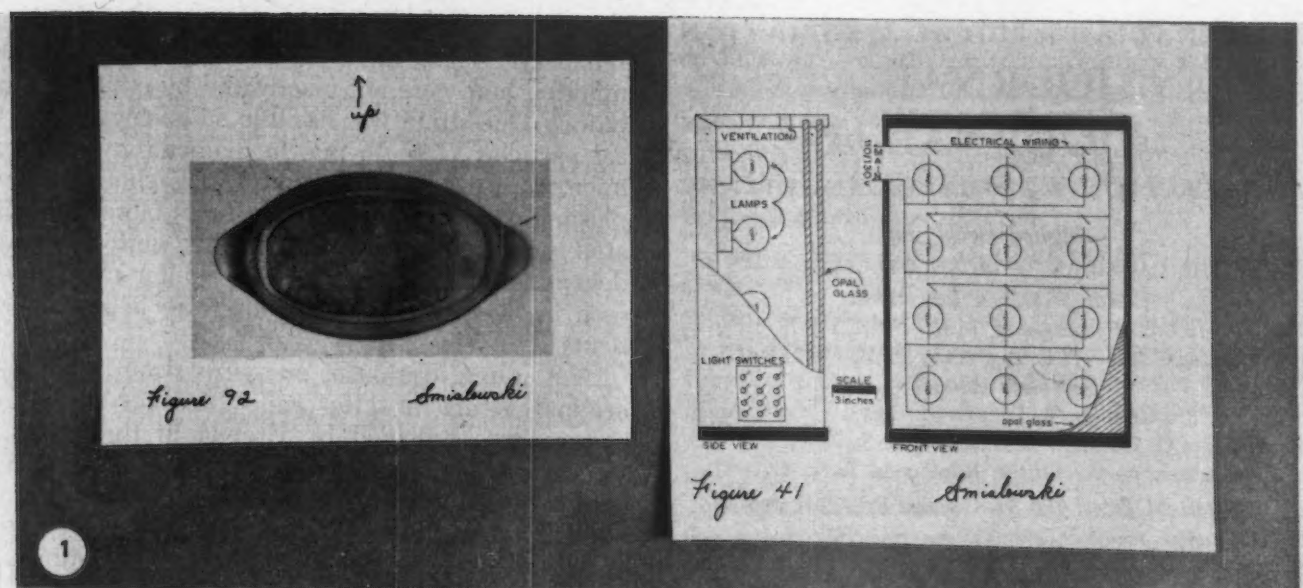


Fig. 3.—Identification and placement of the illustrations in the text. (1) The engraver's proof is approved and the orientation is indicated if it is not obvious. (2) The author's preference for the placement of the illustration is marked on the galley proof of the text. (3) The page proof shows the relationships of the illustration, the legend and the text.

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RECENT HEPATITIS RESEARCH

DESPITE numerous attempts to isolate the causative virus of infectious hepatitis and serum hepatitis during the past quarter century, investigators have failed consistently to induce hepatitis in hosts other than man.¹⁻⁴ In 1956, Rightsel *et al.*⁵ claimed that transmissible agents, cytopathic for the Detroit-6 strain⁶ of human cells in tissue culture, were isolated from cases of infectious hepatitis and serum hepatitis. Other investigators were unable to reproduce these results.⁷ Following recent reports of the isolation of an agent cytopathic for rabbit kidney cell cultures from a pool of icterogenic human plasma,⁸ and agents cytopathic for continuous line tissue cultures of human embryonic lung from 14 of 22 Indian children with infectious hepatitis in Arizona,⁹ accounts of further studies of laboratory characteristics¹⁰ and behaviour in man¹¹ of agents cytopathic for Detroit-6 cells which were isolated from hepatitis patients by Rightsel, Boggs and their co-workers, have been awaited with keen expectancy.

Tissue cultures derived from a cloned strain of Detroit-6 (P.D.) cells were propagated in tubes containing 85% Eagle's Basal Medium and 15% unfiltered bovine fetal serum. After two days' cell growth, the tissue culture supernatant was replaced by an antibiotic-free medium containing 90% Mixture 199 and 10% unfiltered bovine fetal serum. The tubes were inoculated with the sera of patients with hepatitis that had been diluted 1:5, 1:10 and 1:40 and heated at 60° C. for 30 minutes. Cytopathic effects were observed 7 to 12 days after incubation at 37° C. on roller drums, but no cytopathic effect was observed if cultures were incubated for four hours with convalescent-phase sera from hepatitis patients before addition of virus.

Of 24 virus isolates from sera of hepatitis patients, four selected for intensive study were recovered between four days before and five days after onset

of jaundice. All virus strains in serum or plasma remained viable after heating at 60° C. for 30 minutes, and were not inactivated by ether or antibiotics. One strain was filtrable and showed spherical particles 12 to 18 mμ. in diameter by electron microscopy. Infected Detroit-6 cells showed cytoplasmic collections of virus particles closely associated with the ribosomal elements, mitochondrial degeneration and vacuolization, similar to changes seen in liver biopsy specimens from hepatitis patients.

Oral administration of one virus strain, either as original serum or after nine passages in tissue culture, was followed by viremia in three of six subjects, but none developed either neutralizing antibody or evidence of hepatitis. Antibody production without preceding viremia or development of hepatitis was observed in three of six subjects who received another virus strain orally.

Intramuscular administration of one virus strain either as original serum or after passage in tissue culture was followed by viremia in all 20 subjects at intervals between 14 and 63 days after injection. Rising levels of neutralizing antibody were detected in 15 of 20 volunteers by the 84th day, and clinical hepatitis developed in 5 of 20 recipients. Volunteers who had elevated antibody levels to this strain after intramuscular injection frequently developed viremia, rising antibody levels and clinical hepatitis after injection with an antigenically different virus strain. However, the presence of neutralizing antibody did not regularly protect subjects against development of hepatitis after challenge with homologous virus passaged in tissue culture.

Although Rightsel and associates^{10, 11} have reported the isolation of several antigenically distinct agents cytopathic for Detroit-6 cells from sera of patients with infectious hepatitis and the induction of hepatitis following their intramuscular injection into human volunteers irrespective of whether they have pre-existing antibody, further detailed efforts must be directed firstly towards isolation of agents which induce hepatitis regularly after oral administration and secondly to development of agents which induce solid protection against clinical illness after exposure to hepatitis viruses. D.M.M.

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UNUSUAL ENDEMIC DISEASES

DURING the past several years there has been an increasing number of reports of an endemic form of renal disease that has afflicted the inhabitants of some 14 villages in the district of Wraza, in Bulgaria. Between 1954 and 1958, 1160 persons died in these villages, which have a combined population of 18,982. Two hundred and fifty-eight of these deaths were due to an obscure type of renal disease of unknown etiology.¹ This unusual malady affects persons over 20 years of age; and occurs most frequently in the 30 to 60 year age group. Familial occurrence has been evident in 62% of cases. Social and economic conditions in the affected villages are essentially the same as those encountered in neighbouring villages, where no evidence of this disorder could be detected. Loin pain characteristic of renal colic was experienced by 50% of the patients. Urinary findings consisted of moderate albuminuria, frequent hematuria (usually microscopic but sometimes macroscopic) and poor renal concentrating power. Thirty per cent of the patients showed marked pyuria. Uremia was a frequent outcome and the disease was invariably fatal. Despite extensive investigations, no definite etiological agent has yet been elicited.

The changes encountered at autopsy primarily affected the kidneys, which, on the average, were smaller than usual and showed alterations which first involved the tubules and later the interstitial tissue. Of considerable interest was the frequent finding of polyps, papillomas or carcinomas in the renal pelvis, ureters or bladder. Virological studies on 59 patients were unrewarding. The supplies of drinking water in some of the affected villages were subjected to a variety of analyses which failed to disclose any quantitative or qualitative abnormality of metallic content; nor did the soil of these villages contain any demonstrable abnormality of trace elements or radioactivity.

It has been suggested that the endemic "nephritis" reported from some regions of Yugoslavia may be identical with that encountered in the Wraza district of Bulgaria. Yugoslav authorities, by and large, ascribe the endemic form of nephropathy in that country to lead poisoning. While many features of the renal disease endemic in Bulgaria are compatible with lead intoxication, the actual presence of increased concentrations of this metal has been demonstrated in only a small proportion of patients in that country. Furthermore, in a recently published review² of the renal changes in lead poisoning encountered in Yugoslavia, the clinical and biochemical features and natural course in such cases appeared to be quite different from those observed in the Bulgarian form of endemic nephropathy.

An entirely unrelated rare disorder of unknown etiology, paramyloidosis has been encountered in endemic form in the Porto area and northern

coastal region of Portugal, as recently reported by Ardoin and Trincao.³ For many years this disease has been known to affect fishermen of that region, who refer to it as the "maladie des petits pieds", probably because of the associated atrophy of foot muscles due to the neuropathy which is a prominent feature of this disorder.

Approximately 500 cases of paramyloidosis have been recognized in Portugal since 1952. The clinical picture is fairly constant, and, as already noted, its endemic occurrence in that country is striking. Familial trends are prominent; the onset is usually manifested between the ages of 20 and 30 years; and both sexes are affected though it predominates in men. Younger persons tend to suffer more serious and profound forms of the disease. In some instances parents manifest the first signs of paramyloidosis after their progeny have suffered from it for some time. It usually presents in the form of gastrointestinal disturbances such as diarrhea, constipation and occasionally intestinal bleeding; or disorders of sexual function such as impotence, with or without azoospermia in males, or increasing frigidity in females. As a rule, at that stage careful neurological examination will reveal evidence of peripheral neuropathy as manifested by paresthesia and pain. These early neurological changes are followed by gradual impairment of pain and thermal sensation, and later of touch, in the lower extremities, reminiscent of syringomyelia. Eventually paresis, loss of reflexes and muscle atrophy develop and become progressively more pronounced. Loss of bladder and/or bowel sphincter control supervenes and trophic ulcers are frequently observed. If death does not occur at this stage, neurological involvement may progress to complete spastic quadriplegia with contractures. Widespread amyloidosis is evident at autopsy, many of the deposits showing staining properties at variance with those of the amyloid deposits encountered in the more familiar form of secondary amyloidosis. Also, in contrast to the latter, it has not yet been possible to reproduce the Portuguese form of paramyloidosis in animals, by experimental means.

These unusual observations are recorded not only as intriguing epidemiological phenomena but because of the not entirely remote possibility that physicians in Canada might conceivably be confronted by such cases among immigrants from the areas where they are endemic. W.G.

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RESPIRATORY SYNCYTIAL VIRUS

WHILE studying an outbreak of coryza in a colony of chimpanzees, Morris, Blount and Savage¹ recovered a virus which caused syncytia to appear in tissue cultures and which reproduced the disease when inoculated into other chimpanzees. Chanock, Roizman and Myers² subsequently recovered the same virus from children in Baltimore and found some evidence that infection with it was associated with pneumonia. They named the infecting organism "respiratory syncytial (RS) virus". This virus has been the subject of much intensive investigation since that time, and it has now been shown that the RS virus is an important cause of respiratory disease in man. Many of the recent advances in this field have been the result of improvements in methods for recognition of viruses, such as the use of fresh, unfrozen specimens which facilitated the recovery of RS virus.³

Two groups of workers have recently published the results of extensive clinical studies on the effects of this virus. In a controlled study by Chanock and co-workers,⁴ respiratory syncytial virus was recovered from 57% of young infants with bronchiolitis or pneumonia during a five-month period when the agent was prevalent in Washington, D.C. The virus was also recovered from older infants and children with pneumonia or bronchiolitis and from a significant proportion (12%) of young patients with a milder febrile respiratory disease. RS virus infection appeared to occur in sharp outbreaks which lasted three to five months and which coincided with the peak occurrence of bronchiolitis. The three-year serologic experience suggested that 21% of serious lower respiratory tract illnesses in infants and small children was associated with RS virus. These findings suggest that RS virus is a respiratory pathogen of major significance during early life.

Administration of respiratory syncytial virus resulted in infection in 33, and clinical "colds" in 20, of 41 adult volunteers. The incubation period averaged five days, and the illness lasted an average of five and a half days. An association between virus challenge and subsequent illness was supported by the finding that clinical illness never preceded initial RS virus isolation and the fact that illness correlated well with the extent of infection by the virus. Volunteers who became ill generally shed virus for a longer period and were more likely to develop a rise in antibody than infected individuals who did not become ill. It was apparent that RS virus infection in the volunteers represented reinfection, as all of these men had detectable RS-neutralizing antibody prior to challenge with the virus. It is probable that such antibody was responsible for the mild nature of the observed illnesses in these subjects.

Laurella McClelland *et al.*⁵ and Reilly *et al.*⁶ of West Point and Philadelphia have likewise demonstrated by both tissue culture isolations and sequen-

tial antibody determinations that the respiratory syncytial agent is associated with acute febrile respiratory illnesses ranging from mild coryza to bronchitis, bronchiolitis and bronchopneumonia. Much less frequently, it has been isolated from youngsters with croup. In 667 cases of acute respiratory illness in children under the age of 10, RS virus caused the disease in 115 cases (17%). In a control group of 153 cases of non-respiratory illness, three patients (2%) gave positive serodiagnostic results. The commonest signs and symptoms of infection with respiratory syncytial virus were rhinitis, cough, fever and malaise. In about half the cases there was also bronchitis, bronchiolitis or bronchopneumonia. Pharyngitis and conjunctivitis were rare.

It has been estimated that Parainfluenza virus Types 1, 2 and 3 are associated with 15 to 20% of serious lower respiratory tract illnesses in infants and children. In croup these agents are thought to play an even more significant role, being involved in some 50% of cases of this ailment. A recent study suggested that the Eaton agent was associated with 10% of childhood lower respiratory tract illness. Together, the R.S., parainfluenza, influenza, adenoviruses, and Eaton agent may account for as much as 60% of the respiratory illnesses that bring an infant into hospital.

Prevention of RS virus infection by means of a vaccine is under study, but whether it will prove practical or effective is not known at present. The outlook for a satisfactory form of treatment is more remote and is dependent on the development of usable chemotherapeutic agents that are effective against viruses.

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PAGES OUT OF THE PAST: FROM THE
JOURNAL OF FIFTY YEARS AGO

THE PROPRIETARY SCHOOL

There is no longer any profit in running a medical school. The meanest equipment which will suffice for modern needs is more expensive than the installation of other factories from which greater returns can be realized. The average cost of producing a physician in Canada is double the amount of the fees which he pays as a student during his whole course. The medical student now is a burden rather than an asset. The university does not want him *qua* student. It only wants him if he comes in conformity with the university ideal, which is the preservation and advancement of learning. Accordingly, medical schools are now in the habit of boasting that their registration is falling off, the inference being that a heightened standard of entrance and graduation is producing its laudable result.—Editorial, *Canada. M. A. J.*, 1: 1091, 1911.

Letters to the Journal

HYPERCALCEMIA AND MALIGNANT DISEASE

To the Editor:

I would like to confirm the impression given in the excellent article of Dr. O. H. Warwick *et al.* (*Canad. M. A. J.*, 85: 719, 1961) that "physicians still do not appreciate how frequently hypercalcemia appears as a complication of malignant disease". We have made it a practice to present a case discussion at least annually at our rounds to remind physicians of this important and often neglected medical emergency.

To diagnose hypercalcemia regularly requires the following: (1) a physician sensitive to the clinical picture, and (2) a simple and accurate method of determining serum calcium.

The flame photometric method used by the authors is not generally available in smaller hospitals throughout Canada. However, a simple, quick, accurate titrimetric procedure exists which can be adapted for even the smallest hospital laboratories (see Spitzer and Ryan, *Canad. M. A. J.*, 85: 656, 1961, for references). The wider use of this simple chelatometric method should improve the diagnosis of hypercalcemia considerably.

Finally, it has been pointed out (W. P. L. Meyers, *M. Clin. North America*, 40: 871, 1956) that hypercalciuria usually precedes hypercalcemia. Inasmuch as the same simple analytical method can be used for urinary calcium, perhaps it would be worth doing routine urinary calcium determinations on all patients with possible or actual bony metastases, and particularly on those receiving androgen or estrogen therapy.

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BASIC ISSUES IN HOSPITAL AND MEDICAL CARE INSURANCE

To the Editor:

In the September 30 issue (*Canad. M. A. J.*, 85: 799, 1961) Dr. H. E. Emson, in a letter to the Journal under the heading "Basic Issues in Hospital and Medical Care Insurance", writes:

"... we have yet to see 'the right to health' transmitted into 'the duty to be healthy.' Could 'transmitted' be a misprint for 'transmuted'? Failing that, what does the statement mean? Transmitted from what? It must surely be accepted as an aphorism that a person has a duty to society to achieve his maximum of social, physical, and mental health. With this duty is a concomitant right—the right to health. It may well be that I misunderstand Dr. Emson, but I do have difficulty in transmitting a right to a duty, and I have equal trouble with Dr. Emson's concept of seduction by threats.

"But to invite any young man to enter medicine now," writes Dr. Emson, "is to ask him to commit himself and his family to a future of which little can

be discerned, and that little, depressing." I disagree. I have a duty, and hence a right, to say so.

To me, the prospects in medicine have never seemed more bright. That is why I choose to work in that profession. Its future offers, however, no haven of refuge for the person who cannot adapt to change, or indeed for one who likes to work alone. The future in medicine belongs to the team-man, to the man who can recognize that his role as a doctor, though vitally important, is small in the total task of health promotion. In the past such team-work as was done was amongst the doctors themselves.

Further, medicine in the past has been largely a salvage organization. Every item in our fee-for-service schedule has implicit in it the idea that some disease or injury may be present. Doctors have too often been trained through the approach of a technician—find the part that has gone wrong, take it out, repair it, settle a modest and reasonable charge by referral to the appropriate item in the schedule of minimum fees.

Let us honour and respect the men who worked in that professional environment. They were dedicated men of great prestige and personal status. Through the hardships and sacrifices of their daily life they built a public image of the physicians which it is our right to inherit and our duty to maintain.

We can do this only by recruitment to our ranks of young people of vision, people willing to accept changes in the role of medicine that may be more far-reaching than anything of which we can presently conceive. True it is, as Dr. Emson remarks, that little can be discerned of the future of medicine, but this is no cause for depression. It is an exact measure of the size of the social challenge facing a young man of ability, motivated by a desire to serve, eager to join forces with his colleagues in other disciplines, to achieve by a total approach within the social sciences a level of health which it would be impossible to attain by narrow and isolated effort within our own profession.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The gathering together of the profession in greater numbers from time to time, in association meetings, has done much towards creating a better *esprit de corps*. One of the circumstances that have made for a standardizing of operative technic has been the formation of small, clinical, surgical associations, which at various times throughout the year visit from one city to another. There is small reason why such visits should not become international.

There seems to be a growing feeling, the world over, that the most brilliant operator is not of necessity the greatest surgeon. After all, what is more brilliant than an accurate diagnosis with a full knowledge of the pathological condition? Diagnostic methods have improved and will continue to improve; the purely exploratory operation will, ere long, have become a thing of the past.—Retrospect of Surgery, *Canad. M. A. J.*, 1: 1101, 1911.

MEDICAL NEWS IN BRIEF

ERYTHEMA MULTIFORME AND NEPHRITIS

In five patients studied by Comaish and Kerr (*Brit. M. J.*, 2: 84, 1961) erythema multiforme was accompanied by the onset of a form of nephritis manifested by albuminuria, microscopic hematuria, cylindruria, and uremia. Hypertension and oliguria were not features of the acute attack of nephritis in these cases.

Two of the patients died during the acute attack; one progressed to subacute nephritis with chronic uremia; one developed a nephrotic syndrome and subsequently recovered; and in one the renal abnormalities subsided with the rash.

Four of them were treated with corticosteroids: in three the skin rash resolved within a few days of the beginning of treatment, and in one patient the rash recurred during a temporary reduction in steroid dosage. Improvement in the renal condition, when it occurred, was less dramatic and slower, and may well have been coincidental.

It is concluded that an inflammatory renal lesion with some similarity to acute glomerulonephritis accompanies erythema multiforme in a proportion of cases; that it may lead to fatal uremia during the acute illness; and that recurrent episodes may produce chronic nephritis. Further clinical, bacteriological, and histological study is required to determine whether the lesion is identical with the more familiar form of acute glomerulonephritis that follows streptococcal infection. The results of such studies may be important in determining whether long-term prophylactic penicillin is indicated in patients with recurrent attacks.

EFFECT OF HYPERVENTILATION ON RHEUMATOID ARTHRITIS

Symptomatic improvement in rheumatoid arthritis has been observed in situations in which hyperventilation occurs. These include fever therapy, hot baths, certain acute emotional reactions and pregnancy. Conversely, aggravation of symptoms has been observed in situations in which pulmonary ventilation decreases, as during sleep and recumbency. Further, the usual high antirheumatic dose of aspirin exceeds the amount of drug necessary for its maximum analgesic effect in normal persons and usually results in hyperventilation.

A study was undertaken by Kahn, Simmons and Weinberger (*Arthritis & Rheumat.*, 4: 342, 1961) to test the hypothesis that usefulness of aspirin in rheumatic diseases may be related to the biologic effects of hyperventilation. This evaluation was made by comparing some of the effects of aspirin administration with those of hyperventilation induced by the Drinker respirator.

The results of this study are consistent with the hypothesis that the antirheumatic effects of aspirin are related to the biologic alterations associated with severe hyperventilation, since passive hyperventilation with a body respirator simulates some of the clinical and ventilatory effects of massive aspirin therapy.

The usual pitfalls in evaluating clinical response in rheumatoid arthritis are magnified in acute experiments limited to a period of hours. Slight changes

which occurred in swelling, redness and tenderness could not be quantitated or documented satisfactorily with photographs. However, improvement in range of movement was significant and showed no difference between salicylate and respirator hyperventilation. It was apparent also that hyperventilation in the respirator symptomatically improved those patients who were experiencing a severe exacerbation of symptoms after aspirin withdrawal, despite their being immobilized for several hours in one position and subjected to the other discomforts inherent in the use of the respirator.

In this preliminary study, hyperventilation induced by using an iron lung simulated some of the clinical and ventilatory effects of aspirin in 19 patients. The degree of improvement was correlated with the degree of hypocapnia, whether hyperventilation was induced by the respirator or by aspirin. The symptomatic improvement with aspirin was correlated more closely with alveolar $p\text{CO}_2$ levels than with aspirin dosage or serum salicylate levels. These results suggest that the anti-inflammatory effect of aspirin in rheumatoid arthritis may be due to the hyperventilation it causes.

Significant alterations in sedimentation rates occurred after respirator hyperventilation.

The effects of hyperventilation on rheumatoid arthritis are apparently nonspecific and the mechanisms involved remain obscure.

VALUE OF INTRAMUSCULAR TRYPSIN IN ACUTE BACTERIAL PNEUMONIA

The value of intramuscular trypsin as adjuvant therapy in the treatment of acute bacterial pneumonia was explored in a controlled study of 102 patients. Indications of improvement included duration of fever and leukocytosis, rapidity of roentgenographic clearing and duration of hospital stay.

A double-blind study conducted by Moser and Hajjar (*Am. J. M. Sc.*, 241: 423, 1961), comprising 45 patients, did not reveal any significant differences between the clinical or laboratory responses of the two groups. An alternating controlled study including 57 patients similarly failed to demonstrate a favourable effect from trypsin therapy. Within the two groups, there were 79 patients with pneumococcal pneumonia in whom no significant associated disorders existed. Results in these patients were analyzed separately and no appreciable differences in response were detected.

Measurements of plasma antitryptic activity showed no significant change during the period of trypsin administration in 30 patients studied. Plasma fibrinolytic activity was minimally altered during the first four days of observation. Statistically significant changes did occur in those patients who were studied on the fifth and sixth days of trypsin administration, but such changes did not coincide with clinical improvement.

It is concluded that intramuscular trypsin cannot be recommended as adjunctive therapy in acute bacterial pneumonia.

(Continued on advertising page 45)

ASSOCIATION NOTES

THE ANNUAL MEETING OF THE MANITOBA DIVISION: CANADIAN MEDICAL ASSOCIATION

During a convenient hiatus in the Blue Bombers' home schedule, the Manitoba Division held its annual meeting in the Royal Alexandra Hotel, Winnipeg, from October 10 through October 13. More than 225 members of the Manitoba Medical Association and their guests foregathered on this occasion to attend a well-rounded scientific program that included some 18 individual papers, three panel discussions and three medical films.

* * *

After a brief message of welcome from Dr. H. L. McNicol, the outgoing president of the Division, the scientific sessions began with a paper by Dr. C. R. BRADFORD on the subject of *Toxemia in Pregnancy*. In reviewing the trends in therapy during the current century, Dr. Bradford noted that the use of Cesarean section was associated with such a high fetal and maternal mortality that it was ultimately abandoned in the treatment of toxemias except in instances in which this procedure is indicated for other specific reasons. Later, Stroganoff's conservative anticonvulsive regimen gained more favour. Therapeutic programs involving heavy sedation, however, have the following disadvantages: they do not affect the basic mechanisms involved in the genesis of toxemia; they depress maternal and fetal respiratory centres; they do not control blood pressure adequately; some sedatives further depress urinary excretion, which is already impaired in this disorder; and they depress a fetus already jeopardized by poor uterine circulation. A more recent development has been the use of hypotensive, vasodilator drugs to promptly and effectively lower the blood pressure. This form of therapy counteracts the generalized vasospasm that plays an important role in the disordered physiological state of toxemia, avoids maternal respiratory depression and depression of the fetus and controls convulsions. It has been associated with decreased infant mortality due to cerebral hemorrhage and with a lessening of severity of fetal hypoxia. Cardiac and renal failure, common manifestations of toxemia, also are reported to respond favourably to this form of treatment. Hypotensive drug therapy is indicated (a) in the immediate treatment of any severe pre-eclamptic, (b) for all patients in eclampsia, with blood pressures in excess of 150/100 mm. Hg, (c) for pre-eclamptic patients who do not respond to other treatment measures, (d) for hypertensive patients with superimposed pre-eclampsia, and (e) for those showing a sudden rise in blood pressure in the postpartum period. In addition to the accepted general measures of treatment of toxemias, Dr. Bradford recommended the following specific program: (1) administration of 20 mg. of hydralazine (Apresoline) and 5 mg. of cryptenamine (Unitensin) in an intravenous drip of 500 c.c. of 10% glucose in distilled water, at the rate of 20 drops per minute, the blood pressure being recorded every five minutes at first, then every 15 minutes, and the rate of infusion adjusted accordingly; (2) reserpine 2.5 to 5 mg. intramuscularly; and (3) chlorothiazide 1000 mg. initially, followed by 500 mg.

every 12 hours. With this regimen sedation is rarely necessary. Antibiotics are usually indicated for all patients with eclampsia, and in severe cases tracheotomy may be required. This treatment routine requires experience and caution, however. Severe hypotension must be avoided, and vomiting, nasal stuffiness and oliguria occur in some patients so treated. Reserpine may at times be associated with muscle fasciculation. The indications for early delivery are (1) any severe toxemia after the 35th week of pregnancy, (2) increasingly severe toxemia at any stage of pregnancy, if all other measures fail to control this disorder, (3) eclampsia, after convulsions have been controlled for 24 hours, and (4) the presence of such serious complications as placental insufficiency, placental abruption or acute renal failure. It was stressed that prevention is the most important aspect of treatment of toxemia and that the means for its early detection (facilities for urinalyses and recording the weight and blood pressure) are readily available to any physician.

* * *

DR. A. A. EARN, in a discussion of *Self-Administered Analgesia during Labour*, commented that in the past decade more advances have been made in the relief of pain during the first stage of labour than were accomplished in the previous century. Measures designed to alleviate psychosomatic factors, combined with certain pharmacological agents, now provide effective means for the relief of labour pain. Dr. Earn dwelt at some length on the advantages of self-administered gas-air analgesia by means of an apparatus which maintains an unvarying mixture of 50% nitrous oxide and 50% air. Before this device can be used by patients, however, a rather intensive period of prenatal education is essential. In addition to instruction in the technique of self-administration of the gas-air mixture, prenatal education should include an explanation of the anatomy and physiology of labour, the mechanisms and nature of labour pain, and instruction in mental relaxation techniques with the objective of raising the pain threshold during labour. Based on his experience with these procedures Dr. Earn concluded that this technique of gas-air analgesia is remarkably successful in relieving the pain of the first stage of labour, and is a valuable complement to the usual measures used in hospital for this purpose. It is contraindicated only by serious heart, lung or kidney disease. No analgesia can be expected unless the apparatus is used for at least 45 seconds at a time, at the onset of the pain. Even in the second stage of labour, however, it is effective in some cases if used for 60 seconds before each expulsive contraction. The effectiveness of gas-air analgesia is heightened by adequate prenatal psychological conditioning and training in mental relaxation.

* * *

DR. IRENE UCHIDA then presented a lucid and fascinating account of the explosive developments in the field of *Genetics* that have taken place in recent years, and their practical implications in clinical medicine. It was only five years ago that the chromosomes of man were first seen with precision, and their number identified as 46. The startling discovery that mongoloid imbeciles have an extra chromosome in their body

cells was made in 1959. The transmission of this disorder fits no single gene pattern. Repetition is rarely encountered. The presence of this extra chromosome involves the presence of extra genes, the diversity of which accounts for the diversity of the clinical manifestations of mongolism. As a result of this discovery, the presence of a third chromosome complementing the normal pair in the various chromosome groups (trisomy) was sought in other syndromes. As a result of such studies in her department, Dr. Uchida reported the identification of two unusual complexes of congenital anomalies, the so-called "D-Syndrome" characterized by trisomy in the 13-15 group of chromosomes, and the "E-Syndrome" characterized by trisomy of chromosome number 18. Clinically, the D-Syndrome is manifested by hare-lip, cleft palate, polydactyly, hemangiomas, congenital anomalies of the heart and kidneys, and mental deficiency. Clinical features of the E-Syndrome include a small chin, low-set ears, multiple hernias, a huge occiput, congenital deformities of the hands and fingers with overlapping of the other digits by the index, spastic hips, rocker-bottom feet, and congenital anomalies of the heart and kidneys. In one patient who presented these clinical manifestations of the E-Syndrome, an additional X chromosome was also present (the so-called "super-female" pattern), bringing the total chromosome complement in this case to 48. In this patient, a second sex chromatin body was also demonstrable, confirming the fact that this infant possessed a triple-X sex chromosome anomaly. Sex chromosome anomalies such as Turner's and Klinefelter's syndromes, and other syndromes due to various abnormal combinations of X and Y chromosomes, arise by uneven division of chromosomes during the union of ovum and sperm. This process, known as non-disjunction, represents an improper pairing of chromosomes during division of the fertilized ovum. Dr. Uchida enumerated certain clinical aids that may be of value in the diagnosis of disorders due to chromosomal trisomy. Mongolism, for example, can be diagnosed by recognition of typical abnormalities in the pattern of hand and foot prints. Similar characteristic hand and foot print abnormalities have been identified in other abnormal states due to chromosomal trisomy, such as the E-Syndrome.

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DR. ANCEL KEYS, Director of Laboratory and Physiological Hygiene at the University of Minnesota, presented the results of his intensive world-wide studies of *The Risk of Coronary Heart Disease*, in a lecture sponsored by the Manitoba Heart Foundation, noting that from $\frac{1}{4}$ to $\frac{1}{2}$ of all deaths in Canada and the United States, and 80% of all cardiac deaths are due to this disorder. The risk of coronary disease varies greatly among different populations and population groups throughout the world. Study of the factors influencing this risk variation may be of major value in the control and prevention of this disease. Dr. Keys' investigations indicate that age, sex and genetic factors do influence this risk, but these are all factors that are not controllable by means presently available. The prospects of prevention are inversely proportional to the subject's age and duration of coronary atherosclerosis. There appears to be no sound reason to believe that more than a small proportion of cases of coronary disease are due to genetic faults, and it was implied that hitherto too much emphasis has been

placed on the family history, in this regard. The relationship to hypercholesterolemia and cholesterol deposits in the arterial intima appears to offer a promising approach to such a study. In Norway, Finland, the Netherlands and Germany there appeared to be a common pattern of dietary deprivation during the Second World War that was associated with a decrease in coronary disease incidence. Following the war, the restoration of dietary plenty in these countries was paralleled by a concomitant increase in incidence of this disease. The restoration to popularity of the 50-year-old theory that a relationship exists between serum lipid levels and coronary atherosclerosis prompted a number of intensive studies from which interesting findings have emerged, suggesting that there is indeed a relationship between serum lipids, the quantitative and qualitative characteristics of dietary fats and the incidence of coronary atherosclerosis and thrombosis. Studies of four separate population groups in Finland and Yugoslavia indicated that there were no significant differences in these four groups as far as the prevalence and degree of obesity or hypertension were concerned. However, blood cholesterol levels did show significant differences, which correlated statistically with the prevalence of coronary heart disease in the respective groups. Similarly, a co-operative, multi-centre study in the United States revealed that the incidence of "new coronary events" correlated statistically with the incidence of hypercholesterolemia. In three separate population studies in Albany, Los Angeles, and Framingham, Mass., hypercholesterolemia was found to be of significant prognostic value in predicting future coronary disease, whereas obesity and blood pressure showed a much less consistent correlation. Such a relation between serum cholesterol levels and risk of future coronary disease was confirmed in a separate study in Minnesota. It also appears that there is no critical degree of hypercholesterolemia below which there is no increase in coronary risk and that any degree of hypercholesterolemia is associated with a parallel and concomitant rise in risk of coronary heart disease. Previously reported studies that suggested a relationship between coronary risk and occupation (such as the well-known investigation of London bus-drivers and bus-conductors) have been subjected to further analysis, taking into consideration the serum cholesterol levels of the subjects involved. Such re-examination suggests that the blood cholesterol level is of greater significance in predicting coronary heart disease than are the factors of occupation, blood pressure level, degree of overweight, and responsibility and tension inherent in the subjects' work. In one reported Edinburgh study, a group of male subjects were given ethinyl estradiol in doses sufficient to induce manifestations of feminization. After five years' continuous administration at this dosage level there was a significant and sustained decrease in serum cholesterol levels but no significant decrease in coronary disease incidence in the "treated" groups as compared to control subjects. Within three months after administration of this hormone was stopped, there was a uniform "rebound" rise in serum cholesterol to hypercholesterolemic levels. Other similar studies have produced variable results. It has now been established that dietary measures involving alterations in the ratio of saturated to polyunsaturated lipids in the diet provide an effective means of inducing a sustained reduction in serum cholesterol levels. Studies of diet-

ary habits and serum cholesterol levels in Trappist and Benedictine monks have been reported as showing that the serum cholesterol levels behaved as predicted in these two groups of subjects, but there was no evidence of any difference in incidence of hypertension or clinical coronary heart disease between them. However, mortality data in these two groups revealed a statistically highly significant decrease of coronary deaths among the Trappists (who had a low incidence of hypercholesterolemia) as compared with the expected mortality due to this cause.

In summary, the serum cholesterol level appears to be an important factor, but only one of several factors with an influence on predictable coronary risk. To date, there is some doubt that consistent control of the serum cholesterol level will result in significant control of the prevalence of coronary heart disease. Nevertheless, there is still some hope that this may be the case and further intensive studies in this direction appear warranted. This factor and others amenable to control require continued investigation in the interests of effective prevention of this common and serious disease.

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DR. R. A. DETERLING, Surgeon-in-Chief, Pratt Diagnostic Clinic, New England Center Hospital, Boston, reviewed the current measures of *Management of Occlusive Peripheral Vascular Disease*, stressing the need for adequate attention to the vascular system in history taking and physical examination of every patient. The pain of a typical claudication is frequently mistaken for radicular pain due to a disc lesion or for that associated with degenerative joint disease of the hip. In the majority of cases such diagnostic problems can be readily resolved by careful history taking and physical and radiological examination. In addition to systemic factors, such as hypercholesterolemia, that may play a role in the development of atherosclerosis, there are predictable local areas where arterial occlusive lesions are prone to occur as a result of local mechanical, anatomical and traumatic factors. As far as treatment is concerned, thromboendarterectomy is often a worthwhile procedure for thrombotic occlusions proximal to Poupert's ligament. This procedure does thin the vessel wall, however, and may subsequently be followed by aneurysm or rupture of the artery involved. Bypass or replacement graft may therefore be preferable as the operative procedure of choice in such cases. The results of thromboendarterectomy below Poupert's ligament are generally disappointing. Grafting procedures using autogenous vein as an inlay patch are not favoured by most surgeons. Bypass grafts with synthetic prosthetic materials, extending well beyond the area of occlusion, are generally preferred. Homograft material has not proved satisfactory for this purpose; prostheses prepared from crimped Teflon or Dacron enjoy the greatest popularity at present. For short grafts, homologous vein segments may be suitable in many cases. In general, sympathectomy is preferable for those with severe, widespread diffuse arterial disease. For patients with severe pain or rest pain, ulceration and gangrene in the foot or toe, arterial grafting may be carried out for temporary palliation, followed later by sympathectomy. In other cases, sympathectomy may be employed as the initial form of therapy and in a certain proportion of these, the results may be such that subsequent arterial grafting is not necessary. The definitive role of long-term

anticoagulant administration in the treatment of occlusive vascular disease has not yet been established. In young patients with very severe diffuse atherosclerosis with necrosis, ulcerations and pain, subjective relief may be accomplished in some cases by mechanical crushing of the main nerves supplying the affected area. This procedure can also be employed for those who may require subsequent amputation or for those who refuse amputation. When other measures fail and amputation is necessary, this procedure must be carefully planned to meet each patient's individual needs, with a realistic appraisal of his rehabilitation potential.

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DR. R. V. CHRISTIE, Professor of Medicine and Chairman of the Department of Medicine, McGill University, and Physician-in-Chief, Royal Victoria Hospital, Montreal, illustrated his discussion of *Respiratory Resuscitation* by a series of representative case reports. He emphasized that respiratory failure may be an insidious process that is difficult to recognize, and noted that retention of carbon dioxide in the blood may be more dangerous than anoxia, *per se*, and may result in death despite the fact that adequate oxygenation of the blood is maintained. Carbon dioxide narcosis, as such, often escapes diagnosis since it can be very profound in the complete absence of cyanosis. Normally, about 5% of gases in the blood and lungs is CO₂, which is present at a partial pressure of 40 mm. Hg. These figures rise rapidly in the presence of respiratory failure. Acting on the central nervous system, high concentrations of CO₂ have an anesthetic effect and result in drowsiness and irritability, progressing to deep anesthesia, coma and death if the concentration of the gas reaches a sufficiently high level. These manifestations are associated with a concomitant rise in cerebrospinal fluid pressure, which may confuse the diagnosis with that of a cerebrovascular accident or other intracranial lesions. Acting on the cardiovascular system, excessive CO₂ concentrations result in the liberation of adrenaline and noradrenaline, which effect a rise in blood pressure with a full, forceful, rapid pulse. Contrasting effects on the pulse and blood pressure may, however, be exerted by the concomitant central nervous system depression, so that the patient may present a picture resembling shock, with a rapid, thready, feeble pulse and a falling blood pressure. These contrasting effects may exist in varied combinations or one may succeed the other.

Dr. Christie then recounted the case histories of several patients to illustrate the more common types of problems that may be encountered as a result of respiratory failure, the factors involved in its production and the preventive and therapeutic principles involved in such cases. Generally speaking, respiratory resuscitation by means of a mechanical respirator coupled with tracheostomy are indicated for the following types of cases if they are complicated by respiratory failure: (1) those with pulmonary diseases, such as emphysema, asthma, pneumonia or pulmonary fibrosis; (2) postoperative patients—after cardiac or thoracic surgery; (3) those with certain neurological diseases, such as myasthenia gravis, that may be associated with impaired respiratory function; (4) those with toxic states such as barbiturate poisoning or uremia. One of the main attributes of the mechanical respirator is that it now permits the performance of operations on patients with severe pulmonary insuf-

iciency, particularly those with emphysema, who could not survive operation without this device. It was emphasized, however, that such measures of respiratory resuscitation require constant and careful laboratory control which involves the provision of facilities for estimating arterial oxygen saturation and $p\text{CO}_2$. It also involves the performance of frequent arterial punctures, but Dr. Christie remarked that with a little experience this procedure becomes as easy to carry out as venipuncture and entails no greater risk.

DR. R. A. LIM defined the entity of *Gastroduodenal Ulcer* as a form of peptic ulceration in the so-called pyloric channel, involving both gastric and duodenal mucosa. Such lesions are particularly difficult to localize anatomically with accuracy by radiological or other means. They are characteristically associated with a particular symptom complex manifested by marked vomiting and loss of weight. In a series of 84 cases described by Dr. Lim, males were predominantly affected, in a ratio of 7:1, and the sixth decade was the most frequently affected age group. The majority presented with epigastric pain, relieved by food and alkalis, and a periodicity of relief and recurrence. A smaller proportion gave a less typical history of ulcer symptoms. Two-thirds had a history of nausea and vomiting, and 10% complained of nausea without vomiting. These symptoms usually occurred just after meals, and in some cases vomiting was self-induced to relieve pain. Two-thirds of the patients had pronounced weight loss. Fifty per cent had some gastrointestinal bleeding during the course of their disease, varying in severity and frequency. In the majority, gastric acidity with an Ewald test meal was abnormally high. Radiological diagnosis was accurate in the minority of cases in this series. Gastroduodenal (pyloric channel) ulcers probably account for about 10% of all peptic ulcers. The incidence of malignancy in this region is very low, in contrast to that in the prepyloric region of the stomach. For this reason it is important to define the localization of such ulcers with accuracy. In general, the results of operative treatment in this series of cases were satisfactory.

DR. J. F. LIND, in a presentation entitled *Some Aspects of Esophageal Disease*, observed that the diagnosis of disorders of motor function of the esophagus, such as those associated with achalasia, hiatus hernia, scleroderma and diffuse esophageal spasm, is often difficult. He described the studies currently in progress in his department in the investigation of esophageal motility in health and disease with emphasis on techniques for measurement and recording of pressure readings within the esophageal lumen and the sphincters. Disorders of esophageal motor function may be classified as (1) failure to relax (as in achalasia), (2) failure to contract (as in achalasia and scleroderma), (3) incoordination of contraction, and (4) diffuse spasm (frequently associated with hiatus hernia). Dr. Lind presented a series of examples of pressure patterns in these groups of disorders and commented that such motility studies are now becoming a standard form of investigation of non-stenosing lesions of the esophagus.

In presenting his affirmative answer to the hypothetical question, "Are Respiratory Function Tests

Worthwhile?", PROFESSOR R. V. CHRISTIE noted that such tests have gradually been nosing their way into the practice of clinical medicine over the past 10 years. These procedures require trained physicians and technicians as well as extensive space and equipment costing thousands of dollars. Although such facilities are probably not required by all hospitals, it is important that all physicians be familiar with the types of cases in which these tests are of value. Respiratory function tests fall within two broad groups: (1) those that test the efficiency of the thoracic cage in ventilating the lung (vital capacity, maximum breathing capacity and maximum mid-expiratory flow rate), and (2) those that test the efficiency of the lungs in oxygenating blood (lung volume, mixing efficiency, oxygen saturation and $p\text{CO}_2$ of arterial blood, and diffusing capacity). The maximum mid-expiratory flow rate reflects the presence of any obstruction to expiratory flow. The diffusing capacity is a measure of the ability of the lungs to transfer gases from alveoli to blood, usually expressed as the speed with which minute traces of carbon monoxide are so transferred. It is decreased by any process which causes thickening of alveolar walls or damage to the pulmonary capillary bed. Any patient with dyspnea of unknown cause should be subjected to pulmonary function tests. Dr. Christie then recounted illustrative case reports to demonstrate the value of these procedures in establishing an accurate diagnosis and guiding subsequent treatment.

Certain aspects of *Carcinoma of the Lung*, of particular interest and concern to surgeons dealing with this problem, were considered by DR. R. A. DETERLING, who commented on the universal, world-wide rising incidence of such tumours, an increase that has affected males predominantly though it is evident to a lesser extent among women. Ninety per cent of lung carcinomas are reported to occur in men, in persons over 40 years of age, and in those with a history of heavy cigarette smoking over a prolonged period of time. Most authorities consider that there is a clear relation between smoking and lung cancer, although the exact nature of this relationship has not been established. Other etiological factors that appear to have a bearing on lung cancer incidence are heredity, metal fume exposure (particularly to nickel fumes) and air pollution. By the time they reach the doctor most patients are beyond the stage at which they could be considered suitable for extirpative therapy, although Garland has expressed the opinion that about 25% may present with solitary, resectable, pulmonary nodules. In general, about 10% are amenable to pneumonectomy, less than 5% to lobectomy and less than 1% appear to be subjected to exploratory thoracotomy only, without other definitive surgical treatment. Cough, chest pain, hemoptysis, dyspnea, systemic manifestations such as weakness and weight loss, and arthropathy constitute the most common symptoms in that order of frequency and chronology. Routine chest radiographs constitute a diagnostic tool of major importance, and mass radiographic screening surveys have some value, although they also possess definite limitations. Fluoroscopy and laminography are additional useful diagnostic procedures. Angiocardiography may help to assess operability in occasional cases but is of limited value. Bronchoscopy has a diagnostic accuracy of about 40% but is of much less use in cases

of peripheral or alveolar carcinoma. Cytological studies of sputum or material obtained through the bronchoscope are of considerable aid in diagnosis in many cases, though their accuracy varies from one centre to another and with different types, stages of development and sites of tumours. In this respect the fluorescein-orange stain which is picked up by nuclear DNA, and which was introduced by Dr. Bertalanffy, constitutes a useful contribution to cytological studies of this type. Cervical lymph node biopsy is of limited diagnostic value *per se*, and cervico-mediastinal exploration and biopsy appears to be an unduly radical procedure. Careful and adequate thoracotomy is preferable to lung biopsy through a small incision. Dr. Deterling is of the opinion that there is little definite evidence that exploratory thoracotomy without resection increases the morbidity of patients with inoperable lung cancer for the rest of their days or affects their survival significantly. He stressed the difficulties that may be encountered in differentiating between cavitory lesions in abscesses, tuberculous foci and carcinomas, and noted that any two or all three of these lesions may coexist. He mentioned that in selected cases local pulmonary resections of metastatic carcinomas from extrapulmonary primary sites may be of some benefit. It was stressed that age *per se* should not be considered a contraindication to operative resection. The cell type of the tumour does appear to influence the prognosis, squamous cell forms, in general, having the best outlook. Preoperative high voltage radiation of advanced lesions may possibly render occasional pulmonary carcinomas amenable to subsequent resection, though this is probably a rare experience. Chemotherapy appears to have had no significant effect on survival or cure to date, but has a place in palliation in selected cases. Nitrogen mustard is still the most effective chemotherapeutic agent for this purpose. Isolation perfusion and hemi-body perfusion techniques are still in the stages of preliminary investigation and assessment. In concluding, Dr. Deterling stressed the importance of early, definitive, hard-hitting therapy for lung cancer, without undue or avoidable delay. If the tumour in any individual case is ever going to be amenable to surgical resection, the earlier this is done, the better.

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DR. S. K. KAY presented a scholarly and lucid discussion on the subject of *Chest Trauma*, confining his comments to those injuries that involve the ribs, underlying pleura and lung. He emphasized that proper treatment of such cases depends on accurate delineation of the physiological alterations brought about by the injury and the prompt and effective correction of these alterations. When these principles are observed, the result is recovery, in the majority of cases; failure to recognize or delay in recognizing and treating physiological alterations associated with chest injuries very often results in death. Thus, recognition of respiratory insufficiency in chest injury cases is a primary concern, of which the physician must remain constantly aware. Physiological problems in such cases are nearly always *ventilatory* rather than diffusion problems. Most chest injuries predispose to tracheobronchial obstruction due to a variety of causes, including aspirated vomitus, excessive bronchial secretion or bleeding, and obliteration of protective clearing mechanisms, particularly the cough mechanism. As a

result, atelectasis and pulmonary edema may ensue. A simple or closed progressive pneumothorax produces atelectasis by direct compression of the underlying lung. In the presence of an open pneumothorax, if the wound in the pleura is larger than the opening of the glottis, more air enters the hole in the pleura than is inhaled into the lung and the latter is compressed as in the case of an open pneumothorax. If, however, the pleural opening is smaller than that of the glottis, more air will continue to enter the lung, and compression of lung by the pneumothorax will remain minimal. A hemothorax produces physiological effects similar to those of simple or closed pneumothorax. "Flail chest" is a term that applies to injuries in which any portion of the chest wall is completely detached from its skeletal moorings. This portion moves paradoxically with respiration and interferes with normal ventilation. The net result of all of these traumatic conditions is the production of respiratory insufficiency with hypoventilation, decreased arterial oxygenation and carbon dioxide retention. Clinically, these changes are associated with confusion, obstreperousness and rising blood pressure. Dr. Kay enlarged upon the following essential aspects of treatment for patients with chest trauma. (1) Pain may be promptly and effectively relieved by the liberal use of intercostal nerve blocks, extending two rib spaces above and below the site of injury, and repeated every 12 hours. Most patients do not require more than three blocks. Care must be taken to avoid oversedation and depression of the cough mechanism. (2) A clear airway must be maintained. In less severe cases, tracheobronchial suction is adequate for this purpose. If bronchoscopy is repeated too frequently, it may induce further undesirable trauma. If there is any evidence that more than minor tracheobronchial obstruction exists, tracheotomy should be performed; this is probably the most effective single modality of treatment in such cases. (3) Shock must be combated, but it is important to bear in mind that in these cases shock is due to hypoventilation and poses problems in management distinct from those of the shock in other types of trauma, which is due to decreased blood volume. There is a real danger from over-transfusion of patients with chest injuries. (4) Air and/or fluid should be aspirated from the pleural spaces. If bleeding continues or if air continues to re-accumulate, thoracotomy may be necessary. Aspiration should be carried out by intercostal intubation. An open pneumothorax should always be converted into a closed one. (5) If flail chest is present, the chest wall should be stabilized. While most chest injuries without flail chest can be treated simply and conservatively, the severely crushed flail chest is a different problem. Clinical assessment of the degree of crush, the severity of paradoxical respiration, ventilatory insufficiency and anoxemia is inadequate and unreliable, and facilities for accurate measurement of arterial oxygen saturation and $p\text{CO}_2$ are essential for this purpose. Therefore, such cases should preferably be handled in special hospital centres established to deal with such emergencies. These patients require tracheotomy and immobilization of the flail portion of chest wall by strapping, or fixation by wiring. In very severe cases, curare-like drugs may be administered to obliterate the patient's own defective respiratory activity, which is then taken over by a mechanical positive pressure resuscitation apparatus operated by an anesthetist.

DR. C. I. WOOLF reviewed the *Recent Developments in the Surgical Management of Deafness*, confining his comments to the treatment of conductive nerve losses due to otosclerosis and certain other causes. Mobilization of the ankylosed stapes was introduced for this purpose many years ago. In the 1920's the procedure of providing a new window in the labyrinth was developed. 1938 saw the introduction of one-stage fenestration which was subjected to further technical improvements over the subsequent decade. In 1952, the procedure of mobilization of the stapes was "re-discovered" by Rosen, and this technique has since gradually displaced fenestration operations in popularity. Since 1953, further improvements in Rosen's technique of stapes mobilization have been accomplished. The next significant development occurred about 1958, with the introduction of total stapedectomy and replacement of the stapes and its connections with various prosthetic materials such as autogenous vein segments, stainless steel or synthetics such as polyethylene. The main drawback of these radical procedures is the hazard of damage to the cochlear apparatus. Research is in progress to overcome these complications. In general, the simplest procedure calculated to produce a satisfactory result should be selected. Any patient with otosclerosis whose hearing loss is becoming a significant inconvenience should be assessed with a view to deciding whether improvement may be achieved by surgical measures now available. Otosclerosis is the commonest cause of conduction deafness in adult life. This diagnosis can be made with accuracy by simple routine otological examination and Rinne's test. With proper diagnosis and surgical techniques now in use, the results of treatment are becoming progressively more satisfactory, with little risk and few complications. The most common serious complication is loss of cochlear function. Facial nerve paralysis is a rare sequel of such operations. Aside from otosclerosis, the most common cause of conductive deafness is perforation of the drum. If uncomplicated, simple closure of the perforation by electrocoagulation and a skin graft, or an autologous vein graft, is usually satisfactory. If the conductive defect is due to burned-out suppurative middle ear disease with destruction of the ossicular chain, the damaged ossicles can be reconstructed with replacement by a polyethylene prosthesis. Destruction of the ossicles and conduction deafness may follow a head injury or mastoidectomy in childhood, and many of these cases are amenable to surgical reconstruction. The great majority of cases of conduction deafness today can be benefited by some form of surgical treatment and should receive the benefit of careful assessment with this in mind. In a small residual group, however, the mechanisms involved in hearing loss are too complicated or technically complex to respond to the operative procedures that have been developed to date.

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DR. A. R. BIRT commented on *Dermatology Problems* commonly referred to dermatologists from practising physicians. Among those most frequently encountered is contact dermatitis, which may result from the direct chemical action of primary irritants on the skin or may reflect local reactions of the skin to a variety of external irritants on an allergic basis. In the latter instance the diagnosis is based on a careful history and certain laboratory procedures such as

patch testing. Primary irritant dermatitis is, however, the most commonly encountered type of contact dermatitis, and may be due to a wide variety of offending agents such as acids, alkalies, soaps, detergents, items of clothing, waxes or solvents. Dermatitis may result from single or repeated low-grade exposures to such substances which frequently affect persons with fair, delicate skin with minimal sebaceous activity, and those exposed to excessive heat, cold or chapping. It is commonly mistaken for "ringworm" which is then treated by strong applications that invariably make it worse. On the dorsal aspect of the hands and in the interdigital webs the commonest type of eczematous skin lesion is contact dermatitis. This is prone to develop under rings where detergents or other irritants are retained with subsequent maceration of the skin and the development of a chronic dermatitis. Similar lesions may develop beneath ear rings, garters or bracelets. In many such cases the offending primary irritant is a metal, particularly nickel. The diagnosis in these instances may be readily confirmed by a patch test with nickel sulfate. Treatment consists in local rest of the affected part, use of colloidal baths and bland, soothing applications, and organization of the patient's subsequent activities and way of life to avoid further exposure to the primary irritant and to other common irritants such as soap, detergents and soap substitutes. Rubber gloves should be worn when using any cleaning materials, waxes, bleaches, detergents, solvents or the like. Once the skin has cleared, mild soaps (but not detergents) may be used again. In cases of infantile eczema, the actual role of dietary components has not yet been clearly established. Skin testing is of little practical value in this disorder. Egg white is probably the food which most commonly aggravates infantile eczema. Elimination diets are generally of little or no value in the management of infantile eczema and other diagnostic measures should be fully investigated before such dietary regimens are considered. When it is apparent that a particular food, such as egg, is the offender, every product containing that food should be scrupulously eliminated from the diet. If no improvement results after a few weeks on an elimination diet, there is no point in persisting in such a program. In discussing common errors in the diagnosis of ringworm, Dr. Birt noted that this disorder is frequently confused with contact dermatitis, simple interdigital maceration due to hyperhidrosis, infected (pyoderma) eczematoid dermatitis and pustular dermatitis. He noted that the examination of hair for fluorescence under a Wood's light is subject to misinterpretation by the inexperienced. He emphasized that not all skin lesions on the feet are due to epidermophytosis, which is, indeed, not even the most common cause of skin eruptions at this site. Dermatitis on the dorsum of the foot is most frequently a contact dermatitis due to irritants in shoes or socks. Epidermophytosis can be diagnosed definitely only by demonstrating the fungus in scrapings from the lesions. Pustular dermatitis does not respond adequately to simple local applications alone, but usually requires several weeks of continuous systemic treatment with antibiotics or sulfonamides.

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DR. F. M. WOOLHOUSE, Director of the Reparative and Traumatic Unit, Montreal General Hospital, delivered a comprehensive, articulate and effectively

illustrated discourse on the subject of *Hemangiomas and Their Management*. Hemangiomas are hamartomatous malformations, not true angioblastic neoplasms. Based on his observations of 1200 patients with this type of lesion, Dr. Woolhouse commented that the great majority of hemangiomas could be classified simply as: (1) Capillary hemangiomas, bright red lesions frequently developing in the neonatal period, which tend to advance at their periphery and regress at their centres. These accounted for 44% of the hemangiomas in Dr. Woolhouse's series. (2) Cavernous hemangiomas, raised bluish subcutaneous lesions that are compressible on digital pressure and refill when the pressure is released. These are frequently associated with capillary hemangiomas in the overlying skin. Twenty-one per cent of the hemangiomas in this series were of the pure cavernous type. (3) Port-wine stains (5% of this series) are mulberry-coloured capillary lesions usually but not always confined to the dermis and with a predilection for the area supplied by the fifth cranial nerve, for some unknown reason. (4) Mixed capillary and cavernous hemangiomas accounted for the remainder in this series.

This somewhat oversimplified classification omits certain other forms of hemangiomas, such as spider nevi. About 60% of these lesions in Dr. Woolhouse's series were present at birth and another 28% were evident by the end of the first month of life. As far as their treatment is concerned, about 77% needed no definitive surgery in this series, a figure which Dr. Woolhouse considers to be deceptively low. Actually about 90% of capillary and cavernous lesions do not require operative treatment, since they regress spontaneously with gradual fibrosis and obliteration. Sometimes ulceration and infection contribute to their regression, but unfortunately this tends to result in epithelial scarring. In the remaining small group, radiation and/or surgical excision and repair is the treatment of choice. The latter group includes those which progress out of proportion to the patient's age, those which fail to regress and interfere significantly with the function of the part involved and those located in areas prone to ulceration, infection and extensive scarring, such as the buttocks, perineum, vulva and eyelids. Lesions involving mucous surfaces also show a poorer tendency to regression and a higher proportion of these require surgical intervention. Simple surgical excision is the procedure of choice, but it may have to be supplemented by more extensive reconstructive procedures and grafting. Dr. Woolhouse strongly advocated the use of much smaller doses of radiation than those usually used when this modality is employed in the treatment of hemangiomas. He expressed the view that carbon dioxide snow, cautery, diathermy and injection of pigment have, as yet, no place in the treatment of capillary and cavernous hemangiomas.

In his own inimitable style, Dr. E. H. RYNEARSON, Professor of Medicine, the Mayo Foundation for Medical Education and Research, Medical Graduate School, University of Minnesota, Rochester, Minn., delivered an entertaining one-man debate on the question "Which Goitres Are Best Treated with Surgery and Which with Radioactive Iodine?" The gist of his comments was that there are a great number of patients with hyperthyroidism who are better treated by thyroidectomy than by radioisotope therapy. The introduction of tracer

study techniques made it possible to establish definitely that there is such an entity as a hyperfunctioning adenomatous goitre, the existence of which was previously questioned by many. About 20% of large single adenomas and 3 to 5% of multiple adenomas eventually become malignant. This type of patient with a large adenomatous goitre should be treated by thyroidectomy, because no one can predict whether or not such adenomas will or will not become malignant or hyperfunctioning. This opinion, Dr. Ryneerson noted, is not shared unanimously by all endocrinologists, internists or even all surgeons. Astwood, for example, advocates treatment of adenomatous goitres with propylthiouracil, while Crile favours the use of thyroid extract in such cases to suppress secretion of thyroid-stimulating hormone (TSH) by the pituitary gland. For patients over the age of 40 to 45 years of age who suffer from Graves' disease, radioactive iodine in low dosage is the treatment of choice in centres where the patient can return for adequate follow-up and re-treatment if necessary. Where follow-up and re-treatment is not practicable, larger doses of I^{131} can be used; and if myxedema subsequently develops, it can be adequately controlled with replacement thyroid extract. Until the long-term effects of radioactive iodine can be predicted with much greater accuracy, Dr. Ryneerson expressed the view that patients under the age of 40 to 45 years who suffer from Graves' disease should be treated by thyroidectomy after proper pre-operative preparation with iodine or thiouracil derivatives. The risk of leukemia after large doses of radioiodine to young persons is now well recognized. The percentage of serious eye complications after radioiodine therapy is not demonstrably lower than after thyroidectomy, and the mortality from thyroidectomy in patients with Graves' disease, at the Mayo Clinic, has been zero for many years past. Dr. Ryneerson offered the intriguing observation that his comments represent a biased, bigotted opinion which does not necessarily imply that those who oppose his views are wrong although he is sure that they are.

DR. F. M. WOOLHOUSE delivered a detailed, well-illustrated discussion of *Facial Injuries Sustained in Automobile Accidents*, their management, complications and sequelae. The incidence of such lesions is increasing at an alarming rate. Expeditious but complete radiological assessment is of paramount importance in these cases. Early recognition and immediate definitive treatment of the various manifestations of "facial smash" are essential in the interests of best results. The frequent association of such lesions with other injuries requiring urgent surgery, for example neurosurgery, demands a simplified effective approach to the treatment of the facial injuries. Prophylaxis by means of provision and use of seat belts, padded dashboards and other modifications of automobile design was emphasized.

DR. W. L. PARKER reviewed the current state of knowledge concerning the use, effectiveness and safety of *Oral Poliomyelitis Vaccine*. Killed poliovirus vaccines such as the Salk vaccine stimulate antibody formation and, in addition, induce what Salk terms a hyperreactive state that results in a high degree of antibody production when the immunized individual is exposed to subsequent infection by poliovirus. Killed vaccine does not

prevent subsequent infection by poliovirus but prevents or minimizes its effects on the nervous system. Some evidence has been presented suggesting that it is less effective when administered in conjunction with combined diphtheria-pertussis-tetanus vaccine (DPT) than when it is given alone. Live poliovirus vaccine was first used in field trials 10 years ago by Koprowski and later by Cox and by Sabin. World Health Organization authorities consider that Sabin-strain vaccines are the most effective and safest of the attenuated live virus vaccines that have been developed to date. Recently reported trials conducted in the Winnipeg area indicated that among subjects who failed to show a satisfactory antibody response after a routine four-injection course of combined DPT and polio vaccine, an adequate antibody response could be stimulated either by a fifth injection of DPTP or by a course of orally administered live poliovirus vaccine (Sabin). This study indicates that neither immunological immaturity of the vaccinated subjects, immunological tolerance, nor impotent vaccine was responsible for their failure to develop an adequate antibody response after a "four-shot" course of DPTP vaccine. The likely explanation for this failure is the probability that passive antibodies conferred on the vaccinated children by their mothers interfered with their immunological response if they were given Salk vaccine too early in their lives.

Oral poliovirus vaccine possesses the following advantages: (1) The ease of administration (this is of considerable importance in "underdeveloped" countries). (2) It produces intestinal immunity. (3) It induces a rapid antibody response. (4) It prevents "wild" poliovirus infections. (5) Because of (4) it could, theoretically, prevent epidemics. (6) It appears to be safe at all ages (on the basis of observations on some 65 million persons immunized in this way to date). (7) It is not affected by maternal antibodies. (8) It produces lifelong immunity.

On the other hand, it has the following disadvantages: (1) There appears to be some type-inter-

ference when types 1, 2, and 3 poliovirus are given together. (2) For this reason "staggered" feeding of the different types of poliovirus may be necessary. (3) There is no assurance of a "take" in all cases. (4) There is a theoretical risk of neurovirulent reversion of the attenuated virus with re-passage. (5) There is a further theoretical risk of damage to the fetus if it is administered to a pregnant woman, *viz.* abortion, immunologic tolerance or developmental abnormalities. (6) There may be a hazard from latent monkey viruses in the oral preparations now used. So far the theoretical hazards enumerated in (4), (5) and (6) remain to be more fully elucidated but they do not appear to constitute serious risks.

* * *

In addition to the foregoing presentations the program featured the following lively panel discussions, all of which stimulated active participation by the audience in the question period following the panelists' comments: (1) *Recent Advances in Cerebral Vascular Disease* (Chairman—DR. N. C. HILL. Members—DRS. JOHN FARR and R. T. ROSS). (2) *Respiratory Problems in The Postoperative Period and Their Management* (Chairman—DR. D. P. SNIDAL. Members—DRS. M. COHEN, J. T. MACDOUGALL, M. MINUCK and B. SCHOEMPERLEN. (3) *"Compulsory or Voluntary—The Answer?"* (Moderator—DR. L. R. RABSON. Members—DRS. R. L. COOKE, D. N. C. MCINTYRE, K. R. TRUEMAN, and G. E. WODEHOUSE, and MR. B. E. FREAMO). The latter panel discussion, presented in conjunction with one of the official luncheons, created a stimulating exchange of views on the subject of health services insurance and appeared to serve a useful purpose in better informing the general membership of the Manitoba Medical Association of the activities that are being pursued in this field by their Division and by the Canadian Medical Association.

DONALD C. GRAHAM

SUMMARY AND RECOMMENDATIONS OF THE BRIEF TO THE ROYAL COMMISSION ON HEALTH SERVICES FROM THE NEWFOUNDLAND DIVISION OF THE CANADIAN MEDICAL ASSOCIATION

SUMMARY

Health services in Newfoundland have developed more slowly than in other provinces of Canada. Three main factors are responsible for this retarded growth:

- (a) The policy of deliberate discouragement of colonization until the latter part of the eighteenth century.
- (b) The long-continued dispute for sovereignty over large stretches of the Island, concluded only in the 1920's, which hindered stable settlement along the south and west coasts.
- (c) The relative poverty of Newfoundlanders, who have enjoyed only brief periods of anything approaching prosperity in their history.

As a direct outgrowth of these conditions, the development of health services has differed from the pattern established in other provinces of Canada. Lack of local economic self-sufficiency has brought about a heavy involvement of the central governing authority in the provision of hospitals and medical services, and a state of dependency which is unusual in Canada.

As a result, two of the most important health services, provided by the Provincial Government, are peculiar to Newfoundland—the Cottage Hospital Service, providing hospitalization and medical services in the sparsely settled areas of the province; and the Children's Health Service, which provides medical services in hospitals, at government expense, for all children up to age 16.

Thus Government has assumed a substantial interest in the amount and method of payment to doctors. This has resulted in the development of a salaried service for doctors working in the Cottage Hospital Service. Although these doctors formerly regarded themselves as physicians contracting with the Department of Health, a recent edict has classified them as civil servants who must sign and agree to an oath of secrecy.

The Cottage Hospital Service has been a necessary and effective means of providing medical services in outlying areas. It has not, however, provided a sufficient number of doctors to allow necessary improvements in the quality of medical care. Its continued existence in areas of improving economic status is, in our opinion, detrimental to patient care. These areas would be better served if conditions of private practice applied, and to this end we are recommending a method of prepayment of the costs of medical services, with Government assistance.

Our lack of economic self-sufficiency is reflected in the acute shortage of hospital beds of all types and deficiencies in the new and necessary ancillary facilities and personnel. Recent decisions and commitments of our Provincial Government will ease these deficiencies in some areas. We are confident that Newfoundland will become more self-sufficient in the future if our circumstances continue to reflect the same rate of growth as we have experienced in the recent past.

However, today, our deficiencies in health services are many, our financial need is great, and we, the medical profession, cannot foresee that this Province can meet these needs from our existing financial resources. We would present, for your consideration, the following recommendations:

RECOMMENDATIONS

1. *Medical Services Insurance*

We believe that conditions of private practice will attract more doctors than a government salaried service and thus will provide a better quality of care. We recommend that by a process of successive selection all areas of the Province should be encouraged to develop arrangements for the private practice of medicine in their communities. To assist in this endeavour it will be necessary for governments to subsidize local voluntary plans for prepayment of the cost of medical services. The amount of such subsidy should be related to the economic circumstances of each area. (See Paras. 81-88 and 114-115.)

We would recommend for your consideration that the Federal and Provincial Governments should share the amount of subsidy necessary to implement these local plans for prepayment of the cost of medical services.

2. *Mental Health Services* (Paras. 89-91, 104-106, 116-119)

In Newfoundland 900 mental patients are being treated in one mental hospital, an annex and a psychiatric unit, all located in St. John's. Two hundred and fifty of these patients are being housed in accommodation which is below minimum standards. Using as a yardstick the modest total requirement for mental beds of 3.5 beds per thousand, we need an additional 1000 beds for our present population.

Both facilities and personnel are in short supply, so that we have been handicapped in implementing the tremendous new developments in the treatment of mental illness. We are advised that the additional 1000-bed requirement should be implemented by building small hospitals of approximately 200 to 250 beds in St. John's, Corner Brook and Central Newfoundland, plus psychiatric

units, up to 40 beds in size, in each of the larger general hospitals.

We do not believe that the resources of this province are sufficient to provide these additional beds at this time. We are concerned that undue delay will prevent an early introduction of new methods of treating the mentally ill.

We, therefore, recommend for your consideration that the Federal Government should undertake to assume all, or almost all, costs of construction of new beds for the mentally ill. For Newfoundland we estimated that the total capital cost would be 10 to 12 million dollars. The erection of beds would, of course, increase the operating cost of the Provincial Mental Hospitals. The yearly increase would approximate 4.5 million dollars. We would, therefore, further recommend that the operating costs of mental hospitals be accepted by the Federal Government as shareable costs under The Hospital Insurance and Diagnostic Services Act.

3. *Hospital Beds for the Acutely Ill, the Convalescent and the Chronically Ill*

We have outlined deficiencies of 1000 general hospital beds, 500 convalescent beds and 500 beds for the chronically ill (Paras. 99-103, 107-109). Of this number 500 general hospital beds will be built within the next few years and 125 convalescent beds will become available when the Pepperrell hospital is converted. Some easement in the requirement for general hospital beds may be realized when the additional beds for the convalescent and the chronically ill are provided. It is likely, however, that the increase in hospital bed requirements consequent upon the natural population increase will offset these factors. We, therefore, must find, in the relatively near future, \$10,000,000 for the capital cost of additional general hospital beds and \$8,750,000 for the construction of needed beds for the convalescent and chronically ill.

While we believe that our Province can finance these obligations over the long term (with the assistance of present Federal hospital grants), we consider that it is unlikely that funds can be made available at this time over and above the commitments for future hospital bed construction which have already been assumed.

We would, therefore, recommend that this Royal Commission study the possibility of establishing a Federal lending agency to assist in such construction, with repayment of loans over a long term.

We would also recommend that consideration be given to the inclusion of depreciation of hospital buildings as a shareable cost, by the Federal and Provincial Governments, under The Hospital Insurance and Diagnostic Services Act.

4. *Federal Health Grants*

We have commented (Paras. 59-61) that in the past these grants have been very helpful in assisting this Province to up-grade both the quality and quantity of health services in Newfoundland. We recommend that the Commission study methods of extending these grants and augmenting

the funds available so that this method of assisting the Provinces will continue to be as useful in the future.

5. *Other Recommendations*

In this submission we have made a number of additional recommendations which are primarily for the information of the Commission, as implementation will result from continued discussions between our Association and the Provincial Government.

These include:

(a) *Rehabilitation* (Paras. 110-112)

There is a serious lack of rehabilitative facilities and personnel in Newfoundland. We recommend that rehabilitative beds and facilities be established in all larger hospitals in this province. We would expect that this recommendation will be implemented concurrently with the fulfilment of the program we have outlined for needed beds for general hospital, mentally ill, convalescent and chronically ill patients.

(b) *Ancillary Personnel* (Para. 94)

An improved health service for Newfoundland, which would apply if our recommendations are implemented, would urgently require an additional supply of nurses and radiological, laboratory and

other technicians to man the improved and enlarged facilities. We believe that studies should be carried out to determine whether it would be possible for us to train a sufficient number of young Newfoundlanders in this Province to meet this future demand. To this end, we recommend that nursing schools be established in Corner Brook and, subsequently, in Central Newfoundland, and that the training of technicians required be undertaken through the Vocational School system now being established throughout the province.

(c) *Professional Personnel* (Paras. 92-93, 95-98)

The number of doctors practising in Newfoundland has increased substantially in recent years. We believe that the increase would have been greater if conditions of private practice had prevailed throughout the Province. Particularly, we believe that under different circumstances of practice we would have retained a larger proportion of the immigrant physicians who have been attracted to Newfoundland from Britain and Ireland.

We believe that Newfoundlanders, particularly, could be attracted to service in our outlying communities. We would like to see more young Newfoundlanders studying medicine. Because of the heavy financial requirements of a course in medicine, we believe that this objective could be attained by the establishment of a medical school in St. John's and we recommend that consideration should be given to this possibility.

SUMMARY OF THE BRIEF TO THE ROYAL COMMISSION ON HEALTH SERVICES FROM THE PRINCE EDWARD ISLAND DIVISION OF THE CANADIAN MEDICAL ASSOCIATION

SUMMARY

1. We, the Prince Edward Island Division of The Canadian Medical Association, welcome this opportunity to express to you our thoughts on the problem of health in Canada, with special reference to the Prince Edward Island Division. We have placed in your hands a submission which embodies briefly the existing situation in this province as well as suggestions for improvement of the standard of health of the people of this area.
2. We believe that health services provided by private practitioners in this province are of the highest quality, and we are convinced that nothing must be permitted to interfere with the pattern of practice of this group of physicians. This, in essence, requires that the physician-patient relationship must remain undisturbed, that the physician's first responsibility must continue to be to his patient and not to any third party, and that the principle of fee for service must be retained.
3. We believe that many private practitioners, especially in rural areas, are carrying an excessive work load, and we recommend that studies be

initiated into ways and means to facilitate the provision of health services in these areas.

4. Physicians over the years have demonstrated a keen interest in the evolution of prepaid medical care plans. We have reached some definite conclusions regarding the principles which must form the basis of any such plan. These are embodied in the "Statement of The Canadian Medical Association on Prepaid Medical Care Insurance".
5. Government agencies have provided or financed health services in special fields for many years. We believe this policy should be continued, with modifications as necessary, when any province-wide prepaid medical care insurance plan is adopted. In the field of mental health we recommend that every effort be made to promote conditions whereby an adequate and permanent type of psychiatric service may be made available to our citizens. We suggest too that our patients in mental hospitals should not be excluded from the benefits of the Hospital Insurance Plan. We further recommend that facilities be provided for the adequate treatment of alcoholism.
6. While it would appear that there is a shortage of acute care beds in the Summerside area, and of chronic care beds in the Charlottetown area, we believe that the needs in this field, as well as in the field of custodial care beds, are poorly defined and would recommend that further study be given to this problem.
7. We endorse the method of administration of The Hospital and Diagnostic Services Insurance Plan

in this province and urge that this method be retained.

8. To insure an adequate supply of well-qualified physicians for our future needs we urge that, under any circumstances and at all times, conditions must be maintained such that postgraduate study and research are fostered. At the same time the importance of a good public image of the physician cannot be overestimated if recruits are to be attracted to this profession.
9. In proposing a Prepaid Medical Insurance Plan for the people of Prince Edward Island we submit that, to be successful, such a plan must be acceptable to the profession and receive their full co-operation, it must not impede scientific study or research, and it must not interfere with the democratic rights of any citizen. We believe such a plan should be administered by voluntary carriers who can conform to certain specified qualifications, that all necessary in and out of hospital medical service should be covered, that paramedical bene-

fits and extended benefit insurance should also be available, but that these should be administered and funded separately from the necessary purely medical benefits. It is proposed that self-supporting citizens should pay their own premiums while certain other groups will require government assistance in full or in part to enable them to do so. The basis for payment to physicians should be the Schedule of Fees of the Prince Edward Island Division of The Canadian Medical Association, which must remain subject to periodic revision. The projected cost of this plan for all the people of the province at \$20.00 per capita is \$2,000,000, the cost to government is estimated at \$400,000 while self-paying subscribers contribute \$1,600,000. We believe that such a plan has many advantages over any alternate proposal and we submit that, with financial assistance available to those groups requiring it, a large percentage of our population will procure medical care insurance if encouraged to do so.

BOOK REVIEWS

PROGRESS IN MEDICAL GENETICS, Vol. I. Edited by Arthur G. Steinberg. 341 pp. Illust. Grune & Stratton, New York; The Ryerson Press, Toronto, 1961. \$10.75.

This first volume in a new series is one of several excellent reviews of human and medical genetics to appear in the last few months. Its scope can be indicated by listing the contributors and the topics covered: James F. Crow, *Mutation in Man*; J. B. S. Haldane, *Natural Selection in Man*; F. Clarke Fraser, *Genetics and Congenital Malformations*; C. A. Clarke, *Blood Groups and Disease*; Howard Levene and Richard Rosenfield, *ABO Incompatibility*; Donald L. Rucknagel and James V. Neel, *The Hemoglobinopathies*; Newton E. Morton, *Morbidity of Children from Consanguineous Marriages*; and Malcolm A. Ferguson-Smith, *Chromosomes and Human Disease*.

Most of the chapters include both basic scientific considerations and medical applications. For example, Fraser's discussion of congenital malformations begins with a general account on the role of the gene in normal and abnormal development, proceeds to a treatment of genetic and environmental interactions in the etiology of congenital malformations, and concludes with a discussion of the genetics of different specific malformations, which is particularly valuable to clinicians because of its inclusion of recurrence risk figures for genetic counselling.

The enormous amount of information concerning heritable abnormalities of hemoglobin synthesis which has accumulated in recent years illustrates how productive research can become when discoveries in several different areas (here physical chemistry, biochemistry, physiology, genetics, anthropology, and clinical medicine) can be used by workers in other disciplines to illuminate their own fields. The long but selective chapter on the hemoglobinopathies, by Ruck-

nagel and Neel, provides an up-to-date account of this important field.

The chapter on chromosomes and human disease by Ferguson-Smith reviews what is known about abnormalities of chromosome number and structure in relation to disorders of sexual development and congenital malformations, including mongolism. Though it contains little new information, it provides a useful summary for clinicians interested in keeping up with this highly important new field.

The remaining chapters are clearly written and well-balanced accounts by competent authors. The editor is to be congratulated on the selectivity he has displayed in his choice of topics and upon the high quality of the contributions. Under these circumstances it seems unfortunate that a number of trivial but annoying misprints occur, of which the most annoying to this reviewer is the frequent separation of subject and verb by a comma, as for example, "Aird et al., (1960) found a moderately significant excess of group A in 620 patients with cancer of the pancreas."

IMMUNOCHEMICAL APPROACHES TO PROBLEMS IN MICROBIOLOGY. Proceedings of a Symposium Held at the Institute of Microbiology, Rutgers University, September 6-8, 1960. Edited by Michael Heidelberger and Otto J. Plescia. 402 pp. Illust. The Rutgers University Press, New Brunswick, New Jersey, 1961. \$6.00.

This volume contains the prepared papers and the recorded discussions of a symposium held at the Institute of Microbiology of Rutgers University on September 6, 7 and 8, 1960. This was the first of a biennial series planned to consider topics in microbiology, some timely and some perhaps seriously neglected, by groups with divergent background and research orientation. The symposium was organized by

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Drs. Michael Heidelberger and Otto Plescia and the volume was under the editorial supervision of Mr. Robert A. Day. Twenty-seven experts, including nine from countries other than North America, participated in five panels. Each panel consisted of some four to seven papers which are published in this book, with references, followed by discussion by the panelists, comprising seventy-two pages, then by general audience participation. The first panel headed "Quantitative Immunochemical Aspects of Microbial Specificity: Precipitation and Inhibition Techniques" included interpretation of precipitation patterns obtained by diffusion-in-gel techniques, use of immunoelectrophoretic analysis in the study of specific precipitation, separation, and properties of antibodies of high molecular weight, incomplete antibodies, applications of radioactive isotopes to immunochemical studies and quantitative inhibition techniques with oligosaccharides in the elucidation of polysaccharide structure. The second on "Multiplicity and Specificity of Bacterial Antigens" included structure of teichoic acids in bacteria, bacterial antigens and identification by immunoelectrophoretic analysis, mucopolysaccharides of bacterial cell walls, antigens in *Vibrio cholerae* and Group A streptococci. The third on "Immunochemistry of Viruses" discussed tobacco mosaic virus, T-even coliphages, influenza and mouse leukemia viruses. The fourth on "So-called Non-specific Factors in Immunity" considered stimulation of the reticuloendothelial system, immune hemolysis, properties of pig complement, the one-hit theory of immune hemolysis, the properdin system and inhibition in the properdin-dextran system. The final panel on "Biosynthesis of Antigens and Antibodies" included discussions of enzymic synthesis of pneumococcal capsular polysaccharide, a genetic and biochemical approach to the mechanism of capsular synthesis, heterogeneity of globulins produced by plasma cells, antibody formation in the primary and secondary response, disulfide pairing and the biosynthesis of antibody, and the inhibition and restoration of specific immune responses.

The Institute of Microbiology at Rutgers is to be congratulated on the concept of a series of symposia

on broad topics related to microbiology. This, the first one, covered the whole range of immunochemistry, including the remarkable progress that has been made in the elucidation of detailed chemical structure and the limitations of the procedures involved. This volume should be of interest to all microbiologists as well as those working in the immunochemical field.

GENETICS AND OPHTHALMOLOGY. P. J. Waardenburg, A. Franceschetti and D. Klein. 992 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. \$54.50.

This huge, lavishly illustrated, and correspondingly expensive book is the first of a proposed three-volume work which will be a veritable encyclopedia of genetical ophthalmology.

There are 14 chapters, 11 of which have been written entirely by the senior author. The first of these, a chapter on general genetics, is rather unsatisfactory as an introduction to genetics; it contains many errors, e.g. the definition of a genome as "nucleus and chromosomes", the discussion of nucleolar organizers on "the X-chromosome and one of the autosomes" (based upon 1949 work, long before the development of modern cytogenetic techniques), and the term "chromocentre" for Barr's sex chromatin body.

The chapters dealing with clinical ophthalmology appear more accurate, and include an enormous amount of information on many different conditions, taken both from the literature and from the authors' wide experience. The classification is on an anatomical basis.

This book will primarily be valued as a compilation of ophthalmological disorders of genetic etiology. The absence of an index is therefore a disadvantage, even though a detailed table of contents is provided. The lists of references provided at the end of each chapter might have been easier to consult if alphabetical arrangement had been followed for a whole chapter rather than for the separate sections.

The later volumes are to cover neuro-ophthalmology, including stationary functional defects of the retina, progressive neuroretinal abiotrophies, and a number of neuro-ophthalmological syndromes. The completed work will be indispensable to ophthalmologists and to geneticists interested in ophthalmological conditions.

HANDBOOK ON CLINICAL ELECTROMYOGRAPHY. Robert B. Pearson. 72 pp. Illust. The Meditron Company, El Monte, Cal., 1961. \$2.50.

This pamphlet has been designed to serve as an introduction to the field of electromyography. It defines terms and describes the basic histology and physiology, and the patterns observed under various conditions. Types of equipment and techniques are discussed, and standard procedures are briefly mentioned.

It is a practical elementary handbook for a field which is as yet very limited. However, the difficulties in using such equipment and in interpreting the record are not pointed out. Illustrations of nerve and muscle action potentials are good and clear, but the normal confusion pattern produced by voluntary activity is not described.

This book will prove useful in electromyographic laboratories, but is not adequate to take the place of a textbook in the training of physicians in electromyography.

(Continued on page 1126)

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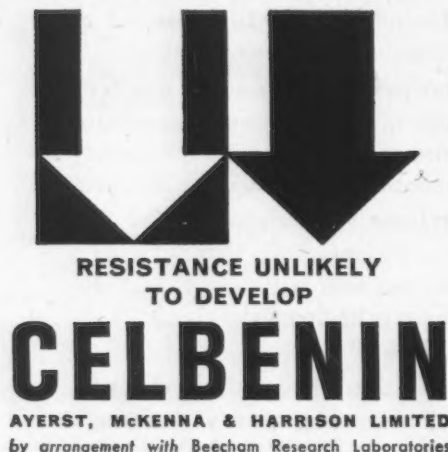
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PLANNING OF PUBLIC HEALTH SERVICES. Fourth Report of the Expert Committee on Public Health Administration, World Health Organization Technical Report Series, No. 215. 48 pp. World Health Organization, Geneva, 1961. \$0.60.

The W.H.O. Expert Committee on Public Health Administration met in Geneva in August 1960 to discuss the planning of public health services. Seven countries were represented by their experts, and the meeting was chaired by Sir John Charles of Great Britain. The present report of this meeting is the fourth of a series. It proves a worthy successor to the first three reports of the committee and should be of interest to all public health administrators.

The planning of public health services is defined as the careful, intelligent interpretation and orderly development of these services in accordance with modern knowledge and experience to meet the health needs of a nation within its resources. National health planning is felt to be an essential part of national development, and it is up to the public health administrators to convince their governments of the need for adequate funds by planning on scientific rather than on largely empirical lines as at present.

The necessity for a preliminary health survey is emphasized. Priorities of action must then be determined. Following this, general targets and objectives have to be set up for the attainment of specific achievements in a specified period of time.

The committee points out quite properly the extreme importance of preliminary consultation with professional organizations. In this way the professional and technical staff have an opportunity to express their views concerning the programs, the successful implementation of which would depend on their efforts. Techniques of evaluation should be built into the plan, and the unique value of annual reports is stressed in this regard.

The report covers a number of points concerning the development of health programs, and in conclusion a plea is made for more so-called "operational research", i.e. the study of administrative or operational problems in public health and more particularly pilot studies at the local, regional and national level with a view to refining planning techniques.

RECOMMENDED REQUIREMENTS FOR SCHOOLS OF PUBLIC HEALTH. Tenth Report of the Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel, World Health Organization Technical Report Series No. 216. 24 pp. World Health Organization, Geneva, 1961. \$0.30.

This tenth report of the Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel should be of particular value to the World Health Organization in its assistance to countries both for the development of their own institutions and for the training of their personnel abroad. It contains much of interest to all schools of public health.

The committee of eight outstanding public health specialists, all from different parts of the world, was provided with material in the form of a questionnaire from most of the existing schools. It is estimated that there are about 60 schools of public health in the world. The 41 schools from which data are available have an enrolment of almost 2500 students. This is felt to be inadequate for the needs.

It is maintained that the training of persons qualified in medicine to work in public health is the main function and common denominator of schools of public health. Also outlined are the various other categories of paramedical personnel trained for work in public health programs.

The committee is of the unqualified opinion that a school of public health which does not carry out research does not meet its obligations, although it is stressed that attention to research should not be pushed so far as to affect unfavourably the teaching and service responsibilities.

Recommendations are made on the content of the major areas of public health: (1) public health administration, (2) health statistics, (3) epidemiology, (4) environmental health and (5) microbiology. It is of interest to note the wide range of time being spent in various forms of teaching with the following averages: lectures 45%, discussions, seminars and visits 20%, laboratory work 21%, and field work 14%.

Some of the major recommendations of the committee are finally summarized under ten headings.

This pamphlet is up to the usual remarkably high standard of W.H.O. publications.

THE ELECTROENCEPHALOGRAM OF THE NORMAL CHILD. Alberto Fois. English ed., translated and edited by Niels L. Low. 124 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1961. \$7.50.

This volume consists of a series of 100 plates, each being a 10-second sample of an eight-channel electroencephalogram of a normal child. The children's ages range from 1 month to 14 years. Both sleeping and waking records are given. Half of the samples are of infants 2 years of age or less.

In the introduction there is a description of the typical characteristics of the electroencephalogram as it develops through childhood. This is clear, concise and adequate.

The book will prove of use to all who are asked to interpret the electroencephalograms of infants and children. This is a difficult field because of the tremendous changes that occur with maturation, and volumes of this type help to guide the student to learn the normal range. It is a book for the electroencephalographer and not for the practising physician who is called upon occasionally to use the electroencephalogram as a diagnostic aid.

MEDICAL NEWS in Brief

(Continued from page 1112)

CANADIAN SOCIETY FOR CLINICAL INVESTIGATION

The Annual Meeting of the Canadian Society for Clinical Investigation will be held at the Royal York Hotel, Toronto, on Wednesday, January 17, 1962.

Abstracts may now be submitted for consideration by the Program Committee. Four copies of each abstract should be submitted to the Secretary before November 15, 1961. Abstracts should be no longer than 250 words and should be factual, concise and informative, so that the objective, nature and results may be gleaned by the reviewer. Contributions of papers for the program are accepted only from members of the Society or contributors whose papers are sponsored by members of the Society.

Investigators with qualifications as set forth in the By-Laws of the Society may be nominated by any two members of the Society. Nominations must be completed and in the hands of the Secretary by November 15, 1961. Application forms will be sent to sponsors on request.

It is suggested to members of the Society that they register at the Royal York Hotel for the meetings and indicate to the hotel that they are participating in the meetings of this Society. This is desirable because the meeting rooms will be made available at a nominal cost if more than 50 members register at the hotel.

Members are reminded that non-attendance at three consecutive meetings, without reasonable excuse, will cause forfeiture of membership in the Society.

Annual dues are now payable in the amount of \$5.00. Immediate submission of dues will aid in avoiding confusion at the time of the Annual Meeting.

The program of the 1962 meeting will include an afternoon symposium on Clinical Investigation in Canada. Dr. Henry Kunkel of the Rockefeller Institute, current President of the American Society for Clinical Investigation, will participate as a guest speaker.

Non-members of the Society may attend scientific sessions of the

(Continued on page 46)

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Charles E. Frosst & Co. tetracycline dosage forms are manufactured in Canada. Subjected to constant and exacting Frosst quality control, "Cefracycline" conforms to the highest pharmacopeial standards.



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DOSAGE: Adults: One tablet four times daily. This dose may be moderately exceeded under special circumstances.

Children: 8 mg. per pound of body weight per day, in divided doses, e.g., children weighing

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60 lb. — $\frac{1}{2}$ tablet four times daily.

Bottles of 16 and 100 tablets



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Each 5 cc. teaspoonful contains tetracycline equivalent to 125 mg. tetracycline hydrochloride.

DOSAGE: Children: 8 mg. per pound of body weight per day, divided into 4 doses, e.g., children weighing

30 lb. — $\frac{1}{2}$ teaspoonful four times daily.

60 lb. — 1 teaspoonful four times daily.

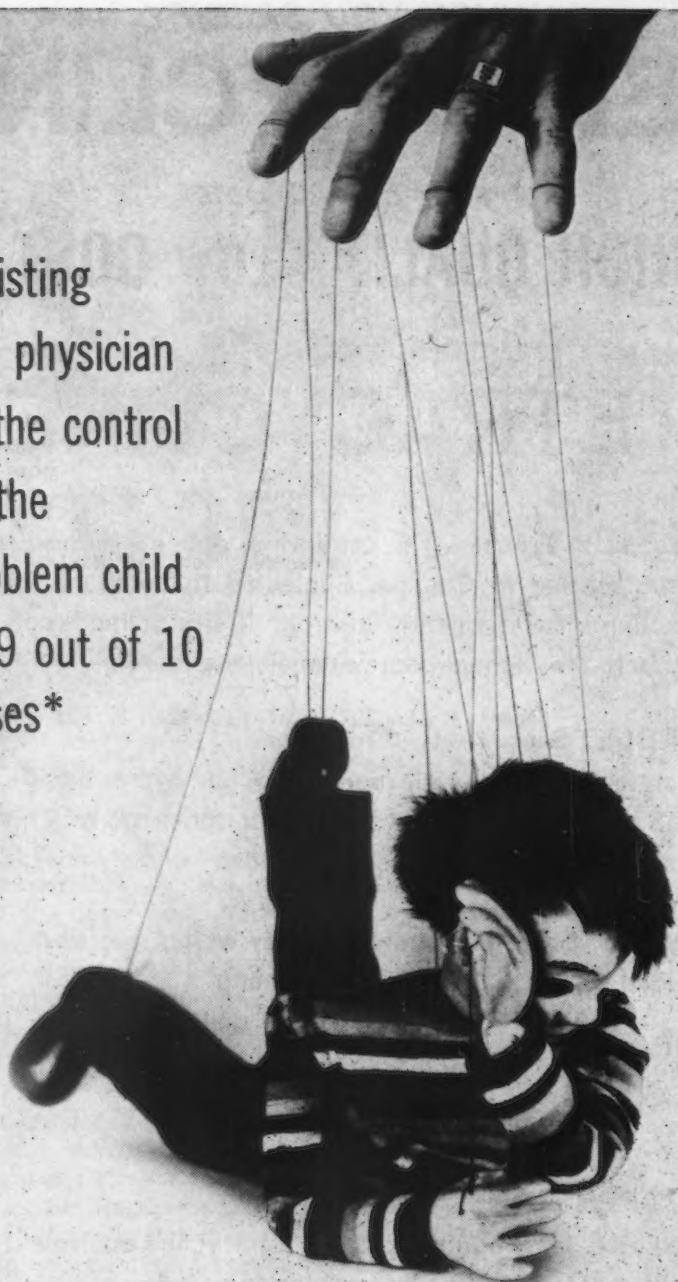
Adults: 2 teaspoonfuls four times daily.

Bottles of 60 cc.

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Each ml. of solution contains 30 mg. MELLARIL.

REF.: M. RENTSCH, *MED. & HYG.* 18: 140, 1960 (transl.)



SANDOZ PHARMACEUTICALS SANDOZ DORVAL, P.Q.

MEDICAL NEWS in brief

(Continued from page 45)

program on payment of a nominal registration fee.

Correspondence should be directed to: R. M. Cherniack, M.D., Secretary-Treasurer, Canadian Society for Clinical Investigation, 111 Medical College, Winnipeg 3, Manitoba.

THE 1961 GAIRDNER FOUNDATION AWARDS

Mr. J. A. Gairdner, President of the Gairdner Foundation, has announced that five medical research workers, one from Canada, two from Britain, one from the U.S.A. and one from Sweden, are being honoured in this year's Gairdner Foundation awards in recognition of outstanding contributions to the treatment of arthritis and heart disease. Each receives a prize of \$5000. The awards were presented to them in person at a testimonial dinner on November 10 at the Royal York Hotel, Toronto.

The names of the recipients and a brief statement of their studies follow.

Alan C. Burton, Ph. D., Professor of Biophysics, University of Western Ontario, in his studies on blood circulation, predicted and verified that blood vessels collapse below a certain blood pressure. He defined the critical opening pressure of blood vessels and the pressure which determines the size of the blood vessels.

Sir Russell Brock, cardiac surgeon at Guy's Hospital and Brompton Hospital, London, England, performed the first mitral commissurotomy in the United Kingdom. He also developed special techniques of cardiac intubation for investigation of cardiac function. Prior to his interest in heart surgery he made significant contributions to the knowledge of lung diseases. In recognition of his work in heart surgery he was knighted seven years ago.

Dr. Jonas H. Kellgren, Professor of Rheumatology and director of the Rheumatism Research Centre, University of Manchester, England, conducted studies in the incidence of rheumatoid arthritis. He has also made significant contributions to the conception of rheumatoid arthritis as a generalized connective tissue disease.

Dr. Alexander B. Gutman, Director, Department of Medicine, Mount Sinai Hospital, New York

City, has furthered understanding of the underlying metabolic defect in gout and has made significant contributions in long-term drug therapy to assist the body in eliminating uric acid.

Dr. U. S. vonEuler, Professor of Physiology, Karolinska Institute, Stockholm, Sweden, distinguished the role of noradrenaline from that of adrenaline in the sympathetic nervous system. This new knowledge has contributed to greater understanding of the heart function and blood circulation. Dr. vonEuler was the first to show in animals that the breathing of air, low in oxygen, causes a rise in pressure and resistance in the pulmonary circulation. The application of this basic observation has been important in the treatment and diagnosis of some types of hypertension.

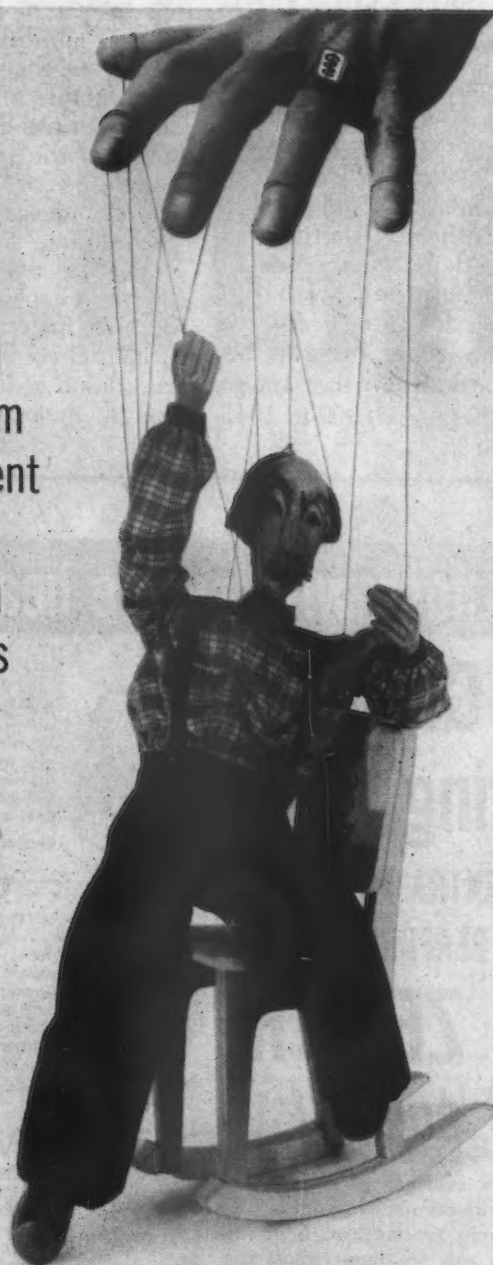
On November 10, the recipients of the awards visited medical departments and laboratories at the University of Toronto, after which a dinner in their honour was held at the Royal York Hotel. On November 11, they are presenting the Gairdner Foundation Lectures at the Toronto General Hospital, Toronto.

HEALTH TRENDS IN CANADA

Health in Canada, judged by longevity data, ranks among the best in the world. The latest official Canadian life tables, relating to 1955-57, show an average length of life of 67.6 years for males and 72.9 years for females. This is approximately at the level of the records for the United States, England and Wales, Australia and New Zealand around the same period. Only the Scandinavian countries and the Netherlands, with much smaller populations, have somewhat better longevity records than Canada.

The pattern of health improvement in Canada is very much like that of other countries of the Western world. Thus, females have not only the lower death rates but also the greater rate of improvement. For males the death rate fell from nearly 12 per 1000 in 1940 to a level of 9.4 in 1954-59; for females, the corresponding decline was from somewhat over 10 to less than 7. Provisional data from the records of Industrial policyholders

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freedom from
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Mellaril, the safe, effective tranquillizing agent for the treatment of mental and emotional disturbances of old age. Mellaril is indicated in senile psychoses, psychoneuroses, cerebral arteriosclerosis, senile brain disease and other conditions involving excitation and anxiety.

* In one longterm study, 75% of the patients benefited from treatment with MELLARIL. No neurological, hepatic or other serious side effects were observed and there was no evidence of drowsiness or interference with the thinking processes.

Average Dose: 30-600 mg. to be adjusted individually
Supply: tablets—10 mg., 25 mg. and 100 mg.
solution—4 oz. bottles with calibrated droppers.

For ease of administration in
geriatrics—NEW MELLARIL SOLUTION.
Each ml. of solution contains 30 mg. MELLARIL.

REF.: V.A. KRAL,
"The Use of Thioridazine (Mellaril) in Aged People"
Can. M.A.J. 84:152 (1961)



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SANDOZ PHARMACEUTICALS SANDOZ DORVAL, P.Q.

MEDICAL NEWS in brief

(Continued from page 47)

of the Metropolitan Life Insurance Company in Canada indicate reductions in mortality from 1959 through the first half of 1961.

Further similarities in mortality trends with other Western countries are found in the records for the leading causes of death. For example, the death rate for the cardiovascular - renal diseases has moved upward from the annual average of 392 per 100,000 in 1941-

45 to 402 in 1959. In like fashion, cancer mortality rose from 123 to 128 over the same period. Significant factors in the increase for each are both the growing proportion of aged in the population and better diagnosis of these diseases with more widespread use of improved techniques.

On the other hand, striking reductions in mortality have occurred for tuberculosis and the principal communicable diseases of childhood (diphtheria, whooping cough, measles and scarlet fever).

For tuberculosis, the death rate fell from an annual average of 50.0 per 100,000 in 1941-45 to only 5.5 in 1959; for the communicable diseases of childhood, the corresponding drop was from 8.7 to 0.8. Equally noteworthy, though not as dramatic, was the improvement in the rate for the aggregate of influenza, bronchitis, and pneumonia, which declined from 69.0 in 1941-45 to 47.2 in 1959. Much more gradual has been the downward trend in accident fatalities, from 60.5 per 100,000 in 1941-45 to 54.1 in 1959.

During the two decades since 1950, infant mortality and the still-birth rate have been cut by about half and maternal mortality by almost 90%. Whereas the infant mortality rate was nearly 60 per 1000 live births in 1940, the figure for 1959 was only 28 per 1000. Meanwhile, the rate for stillbirths fell from 27 to 14 per 1000 live births. Even more spectacular was the reduction in maternal mortality—from 40 per 10,000 live births in 1940 to the very low level of 5.5 in the period 1957-59.

As in all Western nations, the current major health tasks lie in the control of the chronic diseases typical of middle and late life and in measures to reduce accidents. In the present situation, the cardiovascular-renal disorders account for one-half of all deaths in the country, cancer for nearly one-sixth, and accidents for one-twelfth. Another health problem that remains of major importance lies in the relatively high levels of perinatal and infant mortality in some areas, particularly in the eastern provinces.—*Statistical Bulletin*, Metropolitan Life Insurance Co., Vol. 42, August 1961.

EPIDEMIC PLEURODYNIA DUE TO COXSACKIE B-5 VIRUS

During the months of July to October 1958, a widespread outbreak of epidemic pleurodynia (Bornholm disease) occurred in Southern Ontario. In this epidemic three main disease entities were encountered: epidemic pleurodynia, acute benign pericarditis and aseptic meningitis, alone or in combination. The interrelationship of pleurodynia, benign pericarditis

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SUPER R—Features an advanced new Zenith circuit design for outstanding amplification and power, plus improved battery economy in a lightweight instrument. Telemike circuit permits easy use of telephone by eliminating room noises.

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and aseptic meningitis is discussed by Bain, MacLean and Walker (*Pediatrics*, 27: 889, 1961).

Sixty-nine patients were studied at the Hospital for Sick Children, Toronto, and viral studies were carried out for many of them. Five of seven patients with pericarditis had associated pleurodynia, and seven patients had associated pleurodynia and aseptic meningitis. The clinical features of each of the three major entities encountered are presented.

Viral studies point to Coxsackie B-5 virus as the common etiologic agent in the various disease entities encountered in this outbreak. It seems likely that the Coxsackie B virus may be an important etiologic agent in acute benign pericarditis.

Chronic constrictive pericarditis occurred as an end-result in one of the patients with acute benign pericarditis.

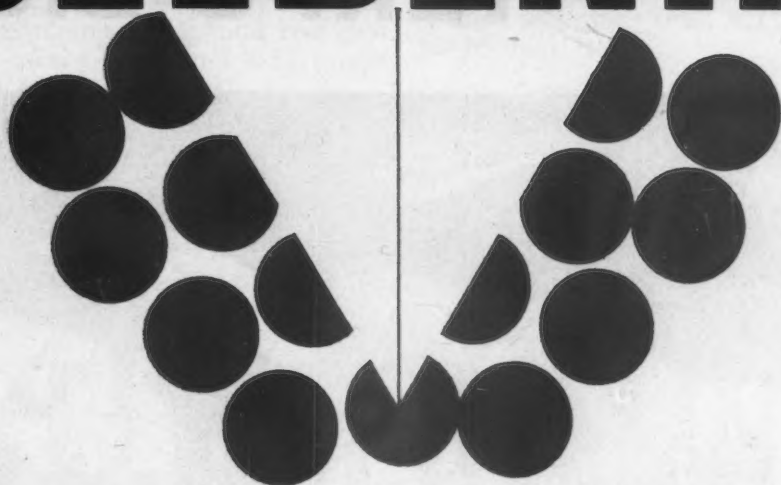
ROENTGEN CHANGES IN REITER'S SYNDROME

Although the triad of urethritis, arthritis and conjunctivitis has been emphasized, many patients with this syndrome also have diarrhea as an early symptom, and others have mucocutaneous lesions. Patients with nonspecific urethritis and arthritis alone have a clinical course indistinguishable from the complete syndrome. Sixty-four patients with Reiter's syndrome, or nonspecific urethritis associated with arthritis, were treated at Walter Reed General Hospital from 1950 to 1960. The roentgenograms of 46 patients were reviewed by Weldon and Scaletter (*Am. J. Roentgenol.*, 86: 344, 1961). The evidence indicates that the syndrome has a consistent roentgenologic pattern.

Changes were most frequently found in the bones and joints of the feet, ankles, and in the sacroiliac joints. The knees were often involved but with no characteristic findings. The hips and shoulders were less commonly involved. In only a few cases were changes in the elbow, wrist, phalanges of the hand, symphysis pubis, and sternoclavicular joint noted. Films early in the course of the illness seldom showed more than periarticular swelling and slight subchondral re-

(Continued on page 51)

BACTERICIDAL TO RESISTANT STAPH CEL BENIN



For serious infection when staph
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More effective than any other
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THE ORIGINAL METHICILLIN FOR RESISTANT STAPH

Comprehensive
"3 Way" Cough Control
 WITH
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induces repose
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ANODYNE

relieves local pain,
 soothes throat area

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facilitates
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The raw, irritated throat and dry, hacking cough accompanied by typical distress and pain become common patient symptoms during Winter, Spring and Fall cough seasons.

TERPO-DIONIN relieves even the most persistent cough, soothes irritated throat

areas, raises exudates and promotes the unbroken rest cough patients need so much.

To enhance the anodyne action of TERPO-DIONIN, patients should be advised to sip each dose, undiluted and hold each sip at the back of the throat before swallowing.

Each fluid ounce of TERPO-DIONIN contains:

Ethylmorphine Hydrochloride (½ gr.)	33.38 mg.
Terpin Hydrate	83.4 mg.
Guaicol	29.4 mg.
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White Pine Compound base.

Available in bottles of 4 oz., 16 oz., 80 oz., 160 oz.



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TERPO-DIONIN is an ORAL PRESCRIPTION
 NARCOTIC product. Pharmacists will be
 happy to fill your telephoned prescription at once.

Winthrop
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 AURORA ONTARIO

MEDICAL NEWS in brief (Continued from page 49)

sorption of the adjacent bone. When symptoms progressed, diffuse demineralization was observed. Many with severe clinical joint symptoms showed bony cortical erosion, periosteal new bone formation, and joint destruction. In the chronic stage, characteristic prolific periosteal new bone formation was noted on the plantar surface of the calcaneus.

Erosions of the articular surfaces were most often seen in the small joints of the feet, knees and sacroiliac joints. Only rarely did the erosion progress to destroy the subchondral cortex, except in the sacroiliac and metatarsophalangeal joints.

Only one patient had severe erosion of the hip joint.

Erosive changes may occur in the calcaneus at the attachment of the Achilles tendon and the plantar fascia, and are always accompanied by pain or tenderness.

Periosteal new bone formation was the most characteristic roentgenographic finding. The characteristic fluffy prolific periosteal reaction on the plantar surface of the calcaneus is believed to be specific for Reiter's syndrome.

A second type of characteristic periosteal new bone formation in this series of Reiter's syndrome was that of linear streaks parallel to the cortex of both the diaphysis and metaphysis of the metatarsals, and especially in the toes.

Although early roentgenographic changes in most joints were generally reversible, sacroiliac joint changes were progressive. Fifteen of 31 patients showed roentgenographic changes in the sacroiliac joints, and these were usually associated with recurrent relapses. Neither the clinical nor roentgenologic manifestations of sacroiliac arthritis are distinguishable with any degree of certainty from those associated with the involvement in rheumatoid arthritis and ankylosing spondylitis. Changes in the spine of the type seen in ankylosing spondylitis were rarely seen in this series of Reiter's syndrome, even when there was destruction of the sacroiliac joints. This differing incidence of spinal changes is an important feature in differentiating these two diseases.

HOSPITAL COSTS

From an analysis of space requirements that appeared in *Canada's Health and Welfare* (16: 3, 1961) and bearing in mind variations in size, hospital costs will range as follows:

The Convalescent Hospital. In the neighbourhood of \$16 to \$21 per square foot. The construction or (b) cost will be between \$7500 and \$9800 per bed. Adding professional fees, furniture, furnishings and equipment, the total cost per bed exclusive of land will range from \$9000 to \$11,800.

The Acute General Hospital. In the neighbourhood of \$17 to \$23 per square foot. Therefore the (b) cost per bed will be between \$11,500 and \$15,750, and total costs per bed exclusive of land will range from \$14,000 to \$19,215.

The Teaching Hospital or the Large General Hospital. In the neighbourhood of \$18 to \$25 per square foot. Therefore the (b) cost will be between \$18,000 to \$25,000 per bed, and total costs exclusive of land will range from \$22,000 to \$30,750 per bed.

(Continued on page 52)

STOPS THE ASTHMA ATTACK IN MINUTES...FOR HOURS... ORALLY

ELIXOPHYLLIN

RAPID RELIEF IN MINUTES—in 15 minutes^{1,2,3} mean theophylline blood levels are comparable to I. V. aminophylline—so that severe attacks have been terminated in 10 to 30 minutes.^{1,4,5,6} **Note:** With Elixophyllin the patient can learn to abort an attack in its incipient stage.

INHERENT SUSTAINED ACTION—After absorption theophylline is slowly eliminated during a 9-hour period.⁷ Clinically *proved* relief and protection day and night with t.i.d. dosage.^{1,3,6,8,9}

NO UNNEEDED SIDE EFFECTS—Since Elixophyllin does not need "auxiliaries," it contains no ephedrine—no barbiturate—no iodide—no steroid. *Gastric distress is rarely encountered.*^{8,9}



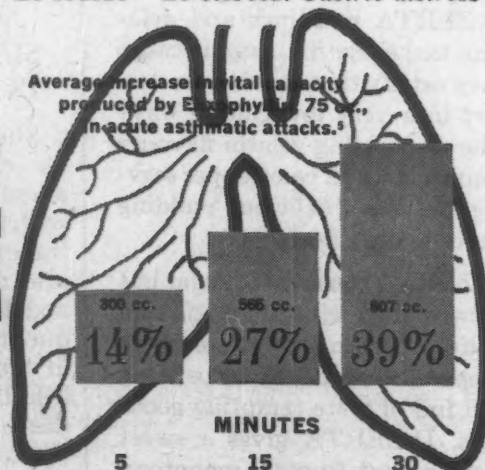
Each tablespoonful (15 cc.) contains theophylline 80 mg. (equivalent to 100 mg. aminophylline) in a hydro-alcoholic vehicle (alcohol 20%).

ACUTE ATTACKS:

single dose of 75 cc. for adults, 0.5 cc. per lb. of body weight for children.

24 HOUR CONTROL:

for adults 45 cc. doses before breakfast, at 3 P.M., and before retiring, after two days, 30 cc. doses. Children, first 6 doses 0.3 cc.—then 0.2 cc. per lb. of body weight as above.



REFERENCES: 1. Kessler, E.: *Connecticut M.J.*, 21:205 (March) 1957. 2. Schlager, J.; McGinn, J.T., and Hennessy, D.J.: *Am. J. Med. Sci.* 233:296 (March) 1957. 3. Kessler, E.: *Med. Times* (Oct.) 1958. 4. Burbank, B.; Schlager, J., and McGinn, J.: *Am. J. Med. Sci.* 234:28 (July) 1957. 5. Spielman, A.D.: *Ann. Allergy* 15:270 (June) 1957. 6. Greenbaum, J.: *Ann. Allergy* (May-June) 1958. 7. Waxler, S.H., and Shack, J.A.: *J.A.M.A.* 143:736 (1950). 8. Bickerman, H.A., and Barach, A.L., in Modell, W.: *Drugs of Choice* 1960-1961, St. Louis, The C.V. Mosby Company, 1960, p. 516. 9. Wilhelm, R.E., Conn, H.F.: in *Current Therapy*—1961, Philadelphia, W.B. Saunders Company, p. 417.

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MEDICAL NEWS in brief

(Continued from page 51)

SEAT BELTS ORDERED FOR U.S. CARS

The General Services Administration has ordered seat belt anchors for passenger safety in federally purchased vehicles and positive crankcase ventilation systems, known as "blowby" devices, to reduce the vehicles' contribution to air pollution. The General Services Administration currently purchases about 7000 new motor vehicles each year.

Luther L. Terry, Surgeon General of the Public Health Service, is quoted by the *A.M.A. News* (August 21, 1961) as saying that "the positive crankcase ventilation systems are highly desirable, reducing total automotive emissions of hydrocarbons by about 25% at a very nominal cost".

"As for seat belts," said Dr. Terry, "the best available statistics indicate that about 5000 lives now being lost annually in automobile accidents could be saved through their universal use. Even more important, perhaps, are the many thousands of permanent disabilities and disfigurements that could be prevented by this means."

Also, seat belts will be installed on some 1000 state-owned vehicles in Nebraska, and state employees will be able to purchase belts at cost for installation on their private cars. And the Tennessee Valley Authority said that it will install belts in its autos when drivers "request and will use them".

SURGICAL OBSERVATIONS IN THE FAR EAST

Studies on the incidence of gastric cancer so common in the Japanese, and on cholangiohepatitis with bile pigment stones in the intrahepatic and extrahepatic ducts, also common among the Japanese and Hong Kong Chinese but infrequently seen in Chinese patients in Singapore or in other Far and Middle Eastern countries and in the United States, are reported by Walters (*Proc. Staff Meet. Mayo Clin.*, 36: 405, 1961).

Cancer of the stomach, peptic ulcer and lesions of the biliary tract were studied in many Japanese hospitals on the Japanese islands of Honshu and Kyushu. Many factors are present in the heredity, food, and drinking habits of this

race of people (who are very thin and eat little animal protein) which, with almost constant thermal irritation of the mucous membranes of the esophagus and stomach by hot rice, tea and saki, may play some role in the high incidence of these lesions. It is not uncommon for Japanese men to drink 15 to 20 cups of hot green tea each day, and rice and rice patties are a large part of each meal. Insufficient vitamins also may be contributory. The number of deaths from cancer of the stomach is high, as the incidence per 100,000 population is five times that in the United States.

Gastric ulcer is much more common than duodenal ulcer in the Japanese, and bile pigment stones occur in much greater frequency in the intrahepatic and extrahepatic bile ducts than do stones in the gallbladder. These are secondary to a cholangiohepatitis resulting from repeated bouts of gastroenteritis that is parasitic in origin in many cases.

Because so many of the Hong Kong Chinese are treated by irregular practitioners using the old, so-

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Canada's First Bank

There are more than 850 B of M
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(Continued on page 56)

to clear **EDEMA...**

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THE STANDARD FOR JUDGING OTHER DIURETICS¹

"Contrary to the prevailing clinical opinion, which holds that the 2-Gm. oral dose of chlorothiazide is as effective as the 2-cc. intramuscular dose of meralluride [MERCUHYDRIN] in patients with congestive failure, the present study shows that it is only about 40% as effective and that it takes an average of two and one-half times as long to clear the edema with chlorothiazide as with meralluride."¹

1. Gold, H., and others: Comparison of Chlorothiazide and with Meralluride, J.A.M.A., 173:745-752 (June 18) 1960.



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MEDICAL NEWS in brief

(Continued from page 52)

called traditional Chinese methods, it is difficult to get reliable statistics referable to the incidence of disease except on estimations based on numbers of patients studied in outpatient departments and in hospitals. Both in Queen Mary's Hospital and Kowloon Hospital cancer of the stomach, although occurring frequently, does not occur with the frequency that it does among the Japanese. However, among the Hong Kong Chinese,

there is a high incidence of esophageal cancer. Studies of cholangiohepatitis and associated bile pigment stones in the intrahepatic and common bile ducts by McFadzean, Stock and Ong seemed to indicate that the *Clonorchis sinensis* infects the upper part of the intestinal tract. From there it is conveyed to the liver by portal blood draining the intestines, producing cholangiohepatitis with biliary calculi. This parasitic infestation is the most prominent etiologic factor in the severe crisis-like attacks of pain with shocklike re-

actions in the Hong Kong Chinese. The chronic attacks of recurring type are similar to those seen in Occidentals. Removal of the stones and drainage of the biliary tract by biliary-intestinal anastomosis have been effective in eliminating or reducing the attacks.

Duodenal ulcer occurs more frequently than gastric ulcer in the Hong Kong Chinese and also in the Chinese of Singapore; on the latter island cholangiohepatitis with bile pigment ductal stones is rarely seen. In the Chinese of both Hong Kong and Singapore, esophageal cancer occurs frequently, but gastric cancer is not as frequent as in the Japanese.

Cancer of the stomach, peptic ulcer, and lesions of the biliary tract among the Vietnamese, the Thais and the people of Northern India (New Delhi) are similar in type and incidence to those in the Occidentals.

SYMPTOM: HEADACHE

PRESCRIPTION:

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CANADIAN OTOLARYNGOLOGICAL SOCIETY:

GEORGE E. HODGE
MEMORIAL AWARD

At its Annual Meeting held in Montreal on June 15, 1961, the Canadian Otolaryngological Society established an Annual Award for the best paper presented by a member of the Society or by a resident of otolaryngology in training.

The purpose of the award is to stimulate the writing of papers by young otolaryngologists. There is no limitation as to subject, which includes all phases of otolaryngology (clinical work, clinical or experimental research).

The award, called the George E. Hodge Memorial Award, is named to commemorate the first President of the Society. It consists of a suitably engraved plaque and a cash prize. The successful author will read his paper at the annual scientific program of the Society. The presentation of the monetary rewards, engraved plaque and attestations will take place at the Annual Meeting.

The manuscript must be typed, double spaced, on letter-size (8½" by 11") paper. The author must not sign his name on the manuscript but must use a pseudonym. His surname and Christian name are to be written in a separate envelope, sealed and sent to the Secretary of the Canadian Oto-

laryngological Society, 174 St. George St., Toronto 5, Ontario, the pseudonym appearing on the outside of the envelope. The closing date for the submission of the manuscript, in triplicate, to the Secretary, is the 31st day of January.

An award committee of three, appointed by the President and his council, will judge the manuscripts and their decision will be final. No award will be given if in their opinion the manuscripts are not worthy of an award. Two awards may be given in any one year. The decision of the Committee will be based upon the scientific and clinical value to otolaryngology, and upon the originality of material.

MULTIPLE PRIMARY BRONCHOGENIC CARCINOMA

Two cases of a second bronchogenic carcinoma developing several years after resection of the original primary bronchial cancer are examined by Hughes and Blades (J. Thorac. Cardiovasc. Surg., 41: 421, 1961). They cite previously reported cases of gross, multiple primary bronchogenic cancer and the evidence for the multicentric origin of bronchogenic carcinoma, and discuss the problem of differentiation between recurrent lung cancer and a new primary lesion.

If a second bronchogenic carcinoma is discovered after a prolonged interval in a patient who appeared to have a successful operation for the original lung cancer, the possibility of a new primary tumour deserves consideration. It is possible in some cases that a resectable new primary cancer of the lung has been considered a hopeless recurrence of the original lesion. In addition to interval roentgen studies, follow-up bronchoscopic examination at six-month to one-year intervals might be an aid in detecting small new primary lesions in the major bronchi. This would be particularly useful in patients treated by lobectomy for epidermoid carcinoma of the bronchus. Cytologic studies might suggest the presence of a new bronchogenic carcinoma.

For example, if lobectomy has been the original procedure, further pulmonary resection for a second primary tumour may be possible. The scope of the opera-

tion would depend on pulmonary status, the location, and the extent of the lesion. A new primary bronchogenic carcinoma in a remaining ipsilateral lobe or main-stem bronchus could be treated by resection of the remaining lobe and main-stem bronchus. In the patient with a small peripheral new primary lesion and pulmonary insufficiency, segmental or wedge resection might be the only applicable type of resection. Following pneumonectomy, resection of a portion of

the contralateral lung would probably have to be confined to segmental or wedge resection. If the second primary tumour were located in the middle lobe, admittedly a rare site, middle lobectomy might be tolerated.

The precise identification and incidence of second primary bronchogenic carcinomas is not well established. The problem of multiple bronchogenic carcinoma will probably, however, become increasingly important.



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PROVINCIAL NEWS

SASKATCHEWAN

The Minority Report presented by Drs. J. F. C. Anderson, C. J. Houston, E. W. Barootes and Mr. D. M. McPherson noted that they were unable to subscribe fully to the Interim Report of the Advisory Planning Committee on Medical Care.

It was pointed out that the Terms of Reference of the Medical Advisory Planning Committee provided for a comprehensive study of all aspects of health services in Saskatchewan. The testimony heard, and studies undertaken by the Committee all seemed to endorse the view that no one aspect of the complex of health services should be considered separately and that improvements on a broad front should be proceeded with as conditions would permit. Assent to the Honourable Mr. Erb's request for an Interim Report on the provision of Medical Services Insurance was given with misgivings. It was felt better for the Committee to complete its studies and so give proper priority to the need for the provision of personal health services by Medical Care Insurance.

The Minority Report felt that much time had been spent on discussions of the meanings of the words "compulsory", "universality" and "universally available", in the context of the Medical Care Insurance Plan for Saskatchewan.

The Committee (as a whole) passed the following resolution:

"The Medical Care Plan shall provide for universal coverage and require all Saskatchewan residents who are able to do so to pay premiums or taxes to finance a plan. The plan shall not require residents or providers of service who do not wish to avail themselves of the benefits of the plan to do so."

Those signing the Minority Report noted that their interpretation of the meaning of this resolution was at variance with the majority who recommended that a plan financed by direct taxation supplemented by public funds from general revenue provide medical care insurance for every resident in Saskatchewan. This view was felt to be compulsory in all its aspects. It was pointed out that taxpayers, who pay substantial taxes, would not continue private medical services insurance nor would the doctors be in a position to withhold their services from insured persons for very long. Economic pressures on both patients and doctors would shortly result in the "state" plan being the only available method of financing personal health services. The Minority Report expressed the view that the quality of medical services provided under state monopoly tended to result in mediocrity and that the regulatory power of the administration under any state plan would be very great. Apprehension was expressed concerning the restrictions likely to be applied to both patient and doctor in the guise of control.

It was pointed out that, in the opinion of those signing the Minority Report, studies should have been given to all types of plans for providing government assistance in the field of medical care prior to the finalization of an Interim Report. Regret was expressed because an opportunity was not provided for further study on the basis of the recommendations proposed by the College of Physicians and Surgeons of Saskatche-

wan. Regret was also expressed that time was not provided to permit a study of the details, implications and costs of the type of plan suggested by the Canadian Federation of Labour.

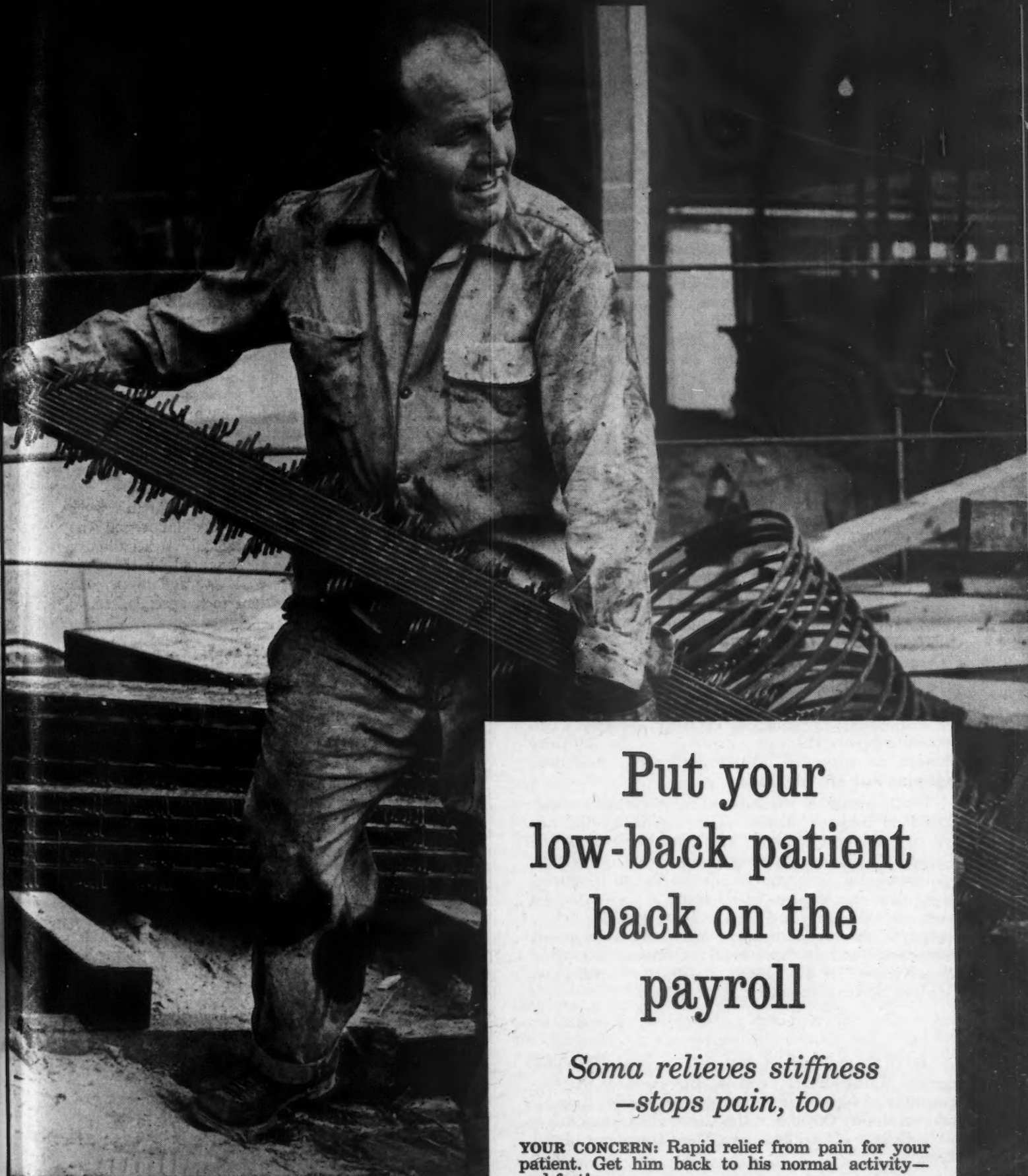
The Minority Report recommended, in place of the monopolistic plan, a system of selective aid to the needy elements of the population in Saskatchewan to permit them to obtain medical services insurance which they would require. This alternative, it was pointed out, had been presented in considerable detail to the planning committee on medical care by several organizations and was felt to fit the needs and resources of the province.

The Minority Report once again pointed out the essentials of a universally available plan as previously recommended which would provide for the self-supporting majority of the people of this province by encouraging them to procure their own medical care insurance through the plans which have been operating successfully over the past years. It was stated that all persons should have free choice to secure insurance coverage which would meet their individual requirements. Public funds should be made available on application in the form of a subsidy to approved carriers for those persons of all ages and limited means who would be unable to finance the premium of medical services insurance, or self-sufficient persons over 65 years of age, in the form of a subsidy. It was pointed out that no distinction should be made between insured persons whose premiums are paid from their own resources and those who are assisted by public funds, and it was emphasized that such a system would achieve universal availability which is desirable. It would provide for more than a single carrier and would also avoid the undesirable features of compulsion and permit the practice of medicine to develop high standards of personal health care. Gradual adjustment by the health profession to the increased demands made upon them would result, and also it would result in a less complex regulating body responsible to the legislature.

It was felt that a selective aid program would best fit the needs and resources of the province. Concern was expressed as to the collective capacity of the taxpayers of the province to finance any plan which might be proposed. Doubt was expressed that the Government and the people of Saskatchewan could assume the extra load of taxation which would be necessary if the recommendations of the Majority Report were adopted and at the same time be in a position to meet the necessary increases of costs required in other health fields.

It had been estimated that a compulsory tax-supported plan of medical care insurance, comprehensive and applicable to all, would cost approximately twenty million dollars in the first year of its operation. Estimates had been presented to the Committee that a selective subsidy program applicable to the needy and currently uninsurable elements of the population would only necessitate an amount of public funds in the order of \$3,600,000 in its first year. It was emphasized that initially such estimates are usually low and that public expenditures where health and welfare

(Continued on page 4)



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(Continued from page 2)

services are concerned would rise progressively, and could only be controlled by curtailment of services.

It was felt that improvements in mental health services deserved immediate attention, and only less urgently, the provision of facilities for the care and rehabilitation of the chronically ill, the aged and the convalescent. Many other deficiencies were said to have been disclosed by the studies of the Committee, and it was pointed out that the claims of equally important health services should not be overlooked in the "current preoccupation" with physicians' services insurance.

After the presentation of the Interim Report to the Government by the Advisory Planning Committee on Medical Care, the Central Health Services Committee of the Saskatchewan College of Physicians and Surgeons met on October 1.

At this meeting the following motion was carried unanimously:

"The proposals outlined in the majority opinion of the Interim Report of the Advisory Planning Committee on Medical Care, concerning physicians' services, are not acceptable to the profession as represented by the Central Health Services Committee."

The Central Health Services Committee also studied the Minority Report which accompanied the Interim Report and passed a motion which was also carried unanimously: "That this Central Health Services Committee supports the views expressed in the Minority Report as presented by Drs. Barootes, Anderson, Houston and Mr. McPherson."

The Committee studied an Administrative Chart based on recommendations as an outline by the Advisory Planning Committee and agreed that while the suggested administrative organization under this type of commission could superficially appear to be attractive, closer examination would reveal a very extensive and effective government control inherent in such a proposal. It would appear that such a proposed Commission did not have fiscal authority or autonomy as advocated in the C.M.A. statement of policy on Medical Services Insurance (Clause 11).

Mr. G. F. Rowbotham, F.R.C.S., Lecturer in Neurosurgery, University of Durham, and Head of the Department of Neurological Surgery, Newcastle, gave an address during October at the University of Saskatchewan, College of Medicine, on "The Circulations of the Brain".

Dr. Hilary Koprowski, Director of the Wistar Institute, University of Pennsylvania, gave a lecture at the University Hospital in Saskatoon on "Resistance to Viral Infections".

On October 25, Professor August B. Hollingshead, Chairman of the Department of Sociology, spoke on "Lower Socio-Economic Status and Schizophrenia".

On October 26, Dr. W. G. Bruce Casselman of the Institute for Muscle Disease in New York spoke on "Some Contributions of Cell Biology to the Study of Muscle Disease".
G. W. PEACOCK

ONTARIO

One of the first two Medical Records Library Schools in Canada was founded at St. Michael's Hospital, Toronto, in 1936; the other was begun at Hôtel-Dieu, Kingston, the same year.

Rev. Sister Mary Paul was the founder of the school at St. Michael's and through the years has been its chief instructress. Her school has contributed 165 graduates to the service of hospitals and other medical institutions throughout Canada. In addition to her teaching, Sister Mary Paul was active in organizing the Canadian Association of Medical Records Librarians and has served on its board of registration. Five St. Michael's hospital graduates have been provincial presidents of this organization and 17 have been presidents of the national organization. One graduate was appointed to serve on a project of revision of the system of medical record keeping in the Federation of Malaya, where she spent two and a half years.

In recognition of her 25 years' service in this work at St. Michael's Hospital, which has influenced the activities of all of Canada's ten Medical Record Library Schools, Sister Mary Paul was honoured by the University of Ottawa with a medal awarded to persons making outstanding contributions in a special field.

The Ontario Public Health Association has named the following officers: President, John Robson, chief sanitary inspector of the Ontario County Health Unit, Pickering; Past-president, Dr. A. V. Hall, Director of Food Control, Department of Health, London; First Vice-president, Dr. G. L. Anderson, Medical Officer of Health and Director, Lambton Health Unit, Sarnia; Second Vice-president, Margaret Cahoon, Associate Professor, School of Hygiene, University of Toronto; and Director-at-large, Dr. A. F. Bull, Medical Officer of Health and Director of Halton County Health Unit.

The Baycrest Hospital Annual Lecture will be held on Monday, November 20, 1961, at 8.30 p.m., in the Baycrest Hospital Auditorium, 3560 Bathurst Street, Toronto. The lecturer will be Dr. Thomas C. Case, Professor of Clinical Surgery, New York Medical College, and Chief of Geriatric Surgery, Bird S. Coler Memorial Hospital. His subject will be "The Changing Trend in Surgery for the Aged". Members of the medical profession and medical students are cordially invited.
LILLIAN A. CHASE

QUEBEC

Dr. G. E. Jayle, Professor of Ophthalmology, Faculty of Medicine, Marseille, France, was guest speaker at a meeting of the Montreal Ophthalmological Society, held at Hôtel-Dieu, Montreal, on September 26. Dr. Jayle spoke on "Examination of the Visual Field in Mesopic Illumination".
JOHN C. LOCKE

CANADIAN ARMED SERVICES

Col. M. Fitch, C.D., of Montreal, has recently been appointed Command Medical Officer at Headquarters, Western Command, Edmonton, Alta.

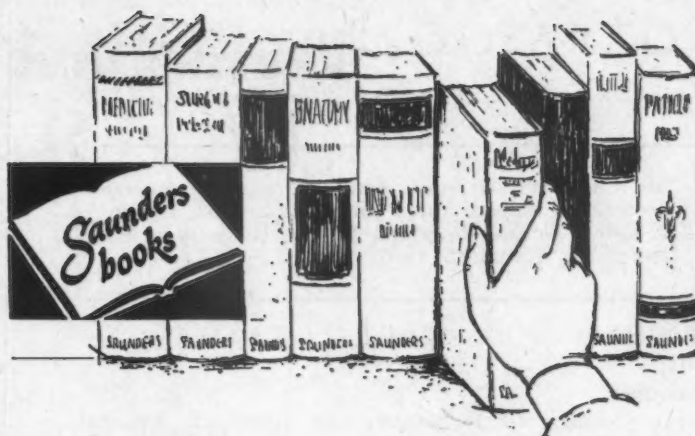
An officer serving with the Canadian Forces Medical Services, Col. Fitch held a similar position at Headquarters, Quebec Command, Montreal.

3 New Editions

Dripps, Eckenhoff & Vandam's Introduction to Anesthesia

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With lucid text and helpful illustrations, this revision clearly illuminates the broad fundamentals of anesthesia and concisely shows specific clinical applications. You'll find indications for various types of anesthesia, the effectiveness of each under different circumstances and the hazards involved in their use. *Inhalation, "open drop," spinal and epidural, intravenous barbiturate and local anesthesia* are all well covered. The authors have thoroughly revised, reorganized and expanded the text to bring you the very latest information—including current drug agents such as recently developed analeptics, the anesthetic agent Halothane, new local anesthetics, etc. You'll find new help on special techniques such as *controlled hypotension, hypothermia, hypnosis, extracorporeal circulation*. You'll find discussions of: the physiological effects of hypercarbia — carbon dioxide absorption — an



approach to asepsis in anesthesia — respiratory resuscitation — pulmonary function — mechanical ventilation — medicine and the law — monitoring during anesthesia. The new cardiac massage procedure is fully described and illustrated.

By ROBERT D. DRIPPS, M.D., Professor and Chairman, Department of Anesthesiology, Schools of Medicine, University of Pennsylvania; Anesthetist, Hospital of the U. of P.; JAMES E. ECKENHOFF, M.D., Professor of Anesthesiology, Schools of Medicine, University of Pennsylvania; Anesthetist, Hospital of the U. of P.; LEROY D. VANDAM, M.D., Clinical Professor of Anaesthesia, Harvard Medical School; Director of Anesthesia, Peter Bent Brigham Hospital, Boston. 413 pages, 6" x 9", illustrated. \$8.00.
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FORTHCOMING MEETINGS

THE CANADIAN MEDICAL ASSOCIATION, 95th Annual Meeting, Winnipeg, Man., June 18-22, 1962. Dr. A. D. Kelly, General Secretary, C.M.A. House, 150 St. George St., Toronto 5, Ont.

CANADA**1961****November**

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS, Regional Meeting, Regina, November 23-24. Dr. Clayton H. Crosby, 2125-11th Avenue, Regina, Sask.

UNITED STATES**November**

AMERICAN COLLEGE OF CHEST PHYSICIANS, Interim Session, Denver, Col., November 25-27. Mr. Murray Kornfeld, Executive Director, 112 E. Chestnut St., Chicago, Ill.

AMERICAN MEDICAL ASSOCIATION CLINICAL MEETING, Denver, Col., November 26-30. Dr. F. J. L. Blasingame, Executive Vice-President, 535 N. Dearborn St., Chicago 10, Ill.

AMERICAN SOCIETY OF HEMATOLOGY, Los Angeles, Calif., November 27-29. Dr. John W. Rebuck, Secretary, Henry Ford Hospital, Detroit 2, Mich.

November/December

RADIOLOGICAL SOCIETY OF NORTH AMERICA, Chicago, Ill., November 26-December 1. Mr. Maurice D. Frazer, Secretary, 3145 O Street, Lincoln, Neb.

AMERICAN MEDICAL WOMEN'S ASSOCIATION, Cleveland, Ohio, November 30-December 2. Dr. Jessie Laird Brodie, Executive Director, 1790 Broadway, New York 19, N.Y.

December

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY, Chicago, Ill., December 2-7. Dr. R. R. Kierland, Secretary-Treasurer, Mayo Clinic, Rochester, Minn.

AMERICAN PSYCHOANALYTIC ASSOCIATION, New York City, December 8-10. Mrs. Helen Fischer, Executive Secretary, 1 E. 57th St., New York 22, N.Y.

ACADEMY OF PSYCHOANALYSIS, New York City, December 9-10. Dr. J. Reed Royce, Chairman, Public Information, 125 E. 65th St., New York 21, N.Y.

OTHER COUNTRIES**December/January**

BAHAMAS SURGICAL CONFERENCE, Nassau, Bahamas, December 27-January 6. Mr. Irwin M. Weschler, Executive Director, P.O. Box 1454, Nassau, Bahamas.

POSTGRADUATE COURSES

THE JOURNAL IS PLEASED TO LIST CANADIAN MEDICAL REFRESHER COURSES OF SHORT DURATION (MINIMUM TWO DAYS, MAXIMUM THIRTY DAYS) THAT ARE DESIGNED TO REFRESH PRACTISING PHYSICIANS IN THE VARIOUS ASPECTS OF THEIR GENERAL MEDICAL EDUCATION, AND TO PROVIDE INFORMATION ON NEW DEVELOPMENTS. THE COURSES LISTED WILL NOT INCLUDE MEDICAL SOCIETY MEETINGS OR PROVINCIAL MEDICAL MEETINGS OF DIVISIONS, HOSPITAL CLINIC DAYS OR THOSE DESIGNED TO PROVIDE INITIAL TRAINING FOR A SPECIALTY

<i>Title of course</i>	<i>Location</i>	<i>Starting date</i>	<i>Ending date</i>	<i>Fee</i>	<i>Apply to</i>
Refresher Course in Pediatrics	"B" Lecture Hall, Faculty of Medicine Bldg., Vancouver General Hospital	November 29	December 1	\$25.00	Dr. R. A. Wilson, Chairman, Post-graduate Education Committee, Vancouver General Hospital, Vancouver, B.C.
Diagnostic Radiology for General Physicians	College of Medicine, University of Saskatchewan	January 8	January 10	\$25.00	Secretary, Faculty of Medicine, Univ. of Sas- katchewan, Saskatoon.
Refresher Course in Medicine	"B" Lecture Hall, Faculty of Medicine Bldg., Vancouver General Hospital	February 14	February 16	\$25.00	Dr. R. A. Wilson, Chairman, Post-graduate Education Committee, Vancouver General Hospital, Vancouver, B.C.
Refresher Course in Surgery	"B" Lecture Hall, Faculty of Medicine Bldg., Vancouver General Hospital	February 12	February 14	\$25.00	Dr. R. A. Wilson, Chairman, Post-graduate Education Committee, Vancouver General Hospital, Vancouver, B.C.
Refresher Course in Anesthesiology	"B" Lecture Hall, Faculty of Medicine Bldg., Vancouver General Hospital	March 26	March 30	\$40.00	Dr. R. A. Wilson, Chairman, Post-graduate Education Committee, Vancouver General Hospital, Vancouver, B.C.
Refresher Course in Obstetrics and Gynecology	"B" Lecture Hall, Faculty of Medicine Bldg., Vancouver General Hospital	April 9	April 11	\$25.00	Dr. R. A. Wilson, Chairman, Post-graduate Education Committee, Vancouver General Hospital, Vancouver, B.C.